METHOD AND MATERIALS FOR INTERPOSITIONAL ARTHROPLASTY IMPLANT

Cross Reference to Related Applications

This application claims priority to U.S. patent application serial number 60/502,003 for Interpositional Arthroplasty Implant and Composition, filed September 11, 2003, U.S. patent application serial number 60/571,305 for Method and Materials for Interpositional Arthroplasty Implant, filed May 14, 2004, U.S. patent application serial number 60/579,695 for Antibiotic Loaded Polymeric Implant, filed June 15, 2004, U.S. patent application serial number 60/584,963 for Test Method for Predicting Wear of Polymeric Devices and Materials, filed July 2, 2004, U.S. patent application serial number 60/588,075 for Tissue Bulking Agent, filed July 15, 2004; US patent application serial number 60/588,878 for Hip Interposition Arthroplasty, filed July 16, 2004, and US patent application serial number 60/592,158 for Method of Predicting Wear from Tensile and Compositional Data, filed July 29, 2004, the contents of each which are hereby incorporated by reference.

Technical Field

In one aspect, this invention relates to materials for implantation and use within the body. In yet another aspect, this invention further relates to the field of orthopedic implants and prostheses, and more particularly, for implantable materials for use in orthopedic joints.

Background Of The Invention

The art is replete with examples of orthopedic implants, including those for use in repairing joints such as the knee. Within this body of literature and patents are included those directed toward the preparation and use of implants for unicompartmental arthroplasty. Applicant itself has previously described, *inter alia*, prosthetic implants formed of biomaterials that can be delivered and finally cured *in situ*, and/or that can be partially or fully prepared *ex vivo*, for implantation into the body, e.g., using minimally invasive techniques. See for instance, U.S. Patent Nos. 5,556,429; 5,795,353; 5,888,220; 6,079,868; 6,140,452; 6,224,630;

6,248,131; 6,306,177; and 6,443,988, as well as US Application Publication Nos. US-2002-0156531; US-2002-0127264; US-2002-0183850; and US-2002-0173852, and International applications having Publication Nos. WO 95/30388; WO 97/26847; WO 98/20939; WO 99/44509; WO 02/17821; and WO 02/17825 (the disclosures of each of which are incorporated herein by reference).

Although biomaterials (materials suitable for use in the body) described to date have demonstrated use, and have opened a new era and related opportunities in joint repair, including interpositional arthroplasty, there remains an ongoing desire for biomaterials having ever improved properties, both with respect to the biomaterials themselves, as well as the overall manner in which they are incorporated or used.

Particularly desired are biomaterials and corresponding implants that provide improved variations and/or combinations of properties suited to particular patient types, including patients that may be more or less active than others, or that may have remaining tissue that is more or less healthy than others.

Summary of the Invention

The present invention relates generally to biomaterials for implantation and use within the body, both in particulate form and for use in implants. The present invention also includes methods of predicting the wear resistance of such biomaterials. More particularly, the present invention relates to biomaterials in orthopedic implants and prostheses adapted to be positioned within (e.g., inserted into) orthopedic joints, in order to provide a weight bearing, articulating, or other mechanical and/or structural feature or function. An exemplary embodiment of the present invention provides an implant suitable for insertion into a joint selected from the group consisting of those that provide immovable articulations (synarthroidal), mixed articulations (amphiarthroidal, e.g., the lumbar joint of the back), and movable articulations (diarthroidal, such as the knee, including both the medial and/or lateral compartments). The ability of amphiarthroidal and diarthroidal joints to provide effective and pain-free articulation, and/or to serve their weight-bearing function, is generally dependent on the presence of intact, healthy fibrocartilage and/or hyalin cartilage within the joint.

An implant in accordance with an exemplary embodiment of the present invention comprises one or more biomaterials adapted to provide an optimal combination of physical-chemical characteristics for a patient's particular needs. The implant can include either a single biomaterial, or more preferably, a composite implant that comprises a plurality of biomaterials, including at least a first biomaterial and a second biomaterial, in a manner adapted to provide an optimal combination of properties. For an articulating, weight bearing joint, for instance, such improved properties include an improved combination of such properties as wear resistance, congruence and cushioning. In some embodiments, the biomaterial is provided with one or more drugs selected to produce a desired effect.

For use in the knee, for instance, a first biomaterial defines a first major surface adapted to be positioned as an articulating surface against a medial condyle of a femur, while the same or a second biomaterial defines a second major surface adapted to mate with the medial tibial plateau of a tibia. Optionally, either or both of these biomaterials can independently be provided by a variety of materials, including for instance, polymers, metals, and/or ceramics. Optionally also, the implant can include one or more additional parts, including one or more, continuous or discontinuous, discrete layers, internal supports, or regions between the first and second surfaces adapted to sufficiently secure the first and second biomaterials to each other, and/or one or more features or components adapted to position and/or secure the implant in a desired manner within or to the joint itself.

A preferred implant remains substantially fixed in position, due in large part to its design and congruence with the tibial plateau, thereby providing for little or no motion relative to the tibial plateau during articulation. Further stabilization can be achieved using various means described herein, including the use of sutures and other such fixation means.

For use in the hip, for example, the present invention comprises an interpositional polymeric hip implant comprised of a biomaterial and adapted to be positioned in the acetabulum and in apposition to a femur to provide a wear and load bearing surface in an arthritic hip joint.

In some exemplary embodiments, the first and second biomaterials of a composite implant meet one another at an interface disposed between the first major surface and the second major surface. In some useful embodiments, the first biomaterial and the second biomaterial are effectively joined or adhered to one another, directly or indirectly, via their interface. In some particularly useful embodiments, the first biomaterial and the second biomaterial are mechanically interlocked with one another. In one such embodiment, the biomaterials are secured together by the use of a support structure provided by or integral to at least one biomaterial and extending into and/or around the other. The interface between the first and second biomaterials, including the optional use of internal supports, mechanical locks, and/or intervening layers of other materials, can be accomplished by any suitable combination of chemical and/or mechanical means.

In some useful, mechanically interlocked embodiments, one of the biomaterials includes at least one protrusion extending beyond the interface. In some implementations one of the biomaterials of a composite implant defines a recess and the other of the parts defines a protrusion fixedly disposed within the recess. In some cases, an enlarged portion of the protrusion is disposed on a second side of the interface and a body portion of the at least one biomaterial is disposed on a first side of the interface.

In some useful embodiments, one of the biomaterials of a composite implant defines a cavity and at least one aperture communicating with the cavity. When this is the case, the other of the parts may advantageously comprise an anchor portion disposed within the cavity, a body portion disposed outside of the cavity, and a plurality of protrusions extending between the body portion and the anchor portion.

In some cases the first biomaterial of the implant may have corresponding properties, including for instance, a first combination of wear resistance, congruence and cushioning, while the second biomaterial has one or more corresponding, and optionally different, properties, including for instance, a second combination of wear resistance, congruence and cushioning, while meeting or exceeding requirements for biocompatibility.

In some cases, for instance, the second biomaterial may comprise a material selected to provide a relatively high level of cushioning, as compared to the first biomaterial, while the first biomaterial may comprise a material selected to provide a high level of wear resistance, as compared to the second. In turn, the first major surface may be advantageously adapted to be positioned as an articulating surface against a medial condyle of a femur. In one such embodiment, the first major surface is preferably dimensioned so as to provide a femoral glide path. Accordingly, the first major surface may include a generally centrally located depression. The second major surface is adapted to mate with the tibial plateau of a tibia, preferably in a substantially congruent and fixed relationship. A preferred composite implant of this type is particularly useful for those patients that retain a high level of mobility and are very active (e.g., joggers). The implant of the present invention can provide the various benefits described herein, e.g., restore alignment, provide a gliding surface for the medial condyle and provide elastomeric cushioning.

In one such preferred embodiment the first biomaterial is selected from the group consisting of metals, ceramics, and polymers having a hardness, in the dry state, of about 60 or more Shore D, together with other suitable properties, while the second biomaterial is selected from the group consisting of polyurethanes having a hardness, in its wet state, of about 60 Shore D or less.

Polyurethane compositions can be modified to achieve a wide range of desired purposes, whether to form an implant of a single material, or as one or more of the biomaterials used in a composite implant. The ingredients and manner of preparation can be modified to achieve a suitable balance between wear resistance, congruence, and cushioning, depending on the role or roles the biomaterial will serve in the implant itself. For use with a single biomaterial implant, for instance, it is preferred that the polyurethane provide for improved fracture toughness, together with congruence and cushioning that are at least acceptable for their intended use. Hence such a polyurethane biomaterial can have a higher hard segment component, as achieved using a higher concentration of isocyanate and chain extender. An example of such a biomaterial is described, for instance, as Compound A in the examples below.

Polymeric biomaterials as described herein can also independently serve as either the first and/or second biomaterials of a composite implant. A polymeric biomaterial for use as the first biomaterial of a composite implant can provide a combination of properties such as improved wear resistance and acceptable congruence and cushioning, as compared to the second, for instance to provide an articulating surface for contact with the femoral condyle of the knee. A polymeric biomaterial for use as the second biomaterial of such an implant can provide a comparable combination of acceptable wear resistance, together with improved congruence and cushioning, for instance, to provide a surface in contact with the tibial bone of a knee.

Brief Description of the Drawing

Figures 1(a) and 1(b) are partial medial side views of a right leg having a single biomaterial implant and composite biomaterial implant, respectively, positioned therein.

Figure 2 (a) shows a top view of an implant in accordance with an additional exemplary embodiment of the present invention.

Figure 2 (b) shows a section view of the implant of Figure 2(a).

Figure 2 (c) shows a section view of the implant of Figure 2(a).

Figure 3 (a) shows a bottom view of an implant in accordance with an additional exemplary embodiment of the present invention.

Figure 3 (b) shows a section view of an implant of Figure 3(a).

Figure 3 (c) shows a section view of an implant of Figure 3(a).

Figure 4 (a) shows a bottom view of a first biomaterial that may form a portion of an implant in accordance with an additional exemplary embodiment of the present invention.

Figure 4 (b) shows a section view of an implant of Figure 4(a)..

Figure 4 (c) shows a section view of an implant of Figure 4(a).

Figure 5 is a cross-sectional view of a mold in accordance with an exemplary embodiment of the present invention.

Figure 6 is an additional cross-sectional view of mold shown in the previous figure.

Figure 7 (a) shows a bottom view of an implant shown in the previous figure.

Figure 7 (b) shows a section view of an implant of Figure 7(a).

Figure 7 (c) shows a section view of an implant of Figure 7(a).

Figure 8 (a) includes a top view of an implant shown in the previous figure.

Figure 8 (b) shows a section view of an implant of Figure 8(a).

Figure 8 (c) shows a section view of an implant of Figure 8(a).

Figure 9 is a perspective view of a first biomaterial that may form a portion of an implant in accordance with an additional exemplary embodiment of the present invention.

Figure 10 (a) includes a top view showing a first biomaterial that may form a portion of an implant in accordance with an additional exemplary embodiment of the present invention.

Figure 10 (b) shows a section view of an implant of Figure 10(a).

Figure 10 (c) shows a section view of an implant of Figure 10(a).

Figure 11 (a) shows a top view of an implant including first biomaterial shown in the previous figure.

Figure 11 (b) shows a section view of an implant of Figure 11(a).

Figure 11 (c) shows a section view of an implant of Figure 11(a).

Figure 12 (a) shows a top view of an implant shown in the previous figure.

Figure 12 (b) shows a section view of an implant of Figure 12(a).

Figure 12 (c) shows a section view of an implant of Figure 12(a).

Figure 13 is a partial front view of a human skeleton including a left leg and a right leg.

Figure 14 is a top view showing a left tibia and right tibia.

Figures 15 (a)-(c) show various views of a further implant as described herein.

Figures 16 (a)-(c) show various views of a further implant as described herein.

Figure 17 shows a perspective view of a hip implant in accordance with an embodiment of the present invention.

Figure 18 shows a perspective view of a hip implant in accordance with an embodiment of the present invention.

Figure 19 shows a perspective view of a tool in accordance with an embodiment of the present invention.

Figure 20(a) shows a top plan view of a tool in accordance with an embodiment of the present invention.

Figure 20(b) shows a cross section view of the tool of Figure 20(a).

Figure 20(c) shows a center cross section view of the tool of Figure 20(a).

Figure 21(a) shows a front plan view of a femoral component in accordance with an embodiment of the present invention.

Figure 21(b) shows a side plan view of a femoral component in accordance with an embodiment of the present invention.

Figure 21(c) shows a top plan view of a femoral component in accordance with an embodiment of the present invention.

Figure 21(d) shows a cross section view of a femoral component in accordance with an embodiment of the present invention.

Figure 21(e) shows a bottom plan view of a tibial component in accordance with an embodiment of the present invention.

Figure 21(f) shows a side plan view of a tibial component in accordance with an embodiment of the present invention.

Figure 22 shows an optical micrograph of a typical surface of an eburnated bone.

Figure 23 shows an abrasive surface compatible for use with Beuhler testing.

Figure 24 is a schematic view of a Buehler test apparatus.

Figure 25 is a plot of predicted wear versus actual wear in accordance with an embodiment of the present invention.

Figure 26 is a plot of wear as a function of rotational speed of the platen in accordance with an embodiment of the present invention.

Figure 27 is a plot of wear as a function of surface roughness in accordance with an embodiment of the present invention.

Figure 28 is a surface plot of wear as a function of inverse elongation and modulus at yield in accordance with an embodiment of the present invention.

Figure 29 is a surface plot of wear as a function of inverse elongation and strain at yield in accordance with an embodiment of the present invention.

Figure 30 is a surface plot derived from an equation in accordance with an embodiment of the present invention.

Figure 31 is a surface plot of wear as a function of composition in accordance with an embodiment of the present invention.

Figure 32 is a contour plot of wear as a function of composition in accordance with an embodiment of the present invention.

Detailed Description

In one preferred embodiment, the method and system involve the preparation and use of one or more components (e.g., polymeric, ceramic and/or metallic that can be at least partially formed outside the body, for insertion and placement into the body. Suitable ceramics include , for instance, bioinert ceramics such as pyrolitic carbon, aluminum oxides, zirconia ceramics, hydroxyapatites, and calcium aluminates, while suitable metals include, for instance, stainless steels, cobalt chromium alloys, titanium and its alloys, and tanatalum. See, respectively "Ceramic Biomaterials", pp 38-1 to 38-33 and "Metallic Biomaterials", pp 37-1 to 37-20, in The Biomedical Handbook, 2nd Edition, CRC Press 2000, the disclosures of which are incorporated herein by reference. The method and system permit the previous manufacture of a unicompartmental interpositional arthroplasty device that comprises a polymeric material such as polyurethane.

In a related and particularly preferred embodiment, the implant can be prepared (including fully cured) *ex vivo*, for later implantation. In a particularly preferred embodiment, as described below, the present invention therefore provides an implant that is designed to be formed to and congruent with the tibial surface, having a final femoral surface shape that serves largely as a glide path with respect to the femoral condyle. Such a device can be used in patients having joints that have progressed to the stage of "bone on bone" osteoarthritis, and thus provides a replacement for the function of articular cartilage, and optionally some of the natural meniscus, and particularly at the central weight-bearing area, in order to restore alignment, providing an elastomeric, cushioning function. A preferred implant of this type is also congruent with the tibial surface, based upon both its initial shape, together with whatever final shaping and/or joint preparation may occur. In turn, the

present implant is more permanently and fixedly stabilized in position, in significant part by one or more posterior projections, such as the posterior lip, as well by the optional but preferred use of anterior fixation means (such as, for example, embedded sutures). In addition, stabilization may be assisted by congruence to the tibial plateau, and/or the presence of anterior features such as a wedge or lip.

The invention will be further described with respect to the Drawing, in which figure 1 is a partial medial side view of a right leg 100. Right leg 100 includes a femur 102, a tibia 104, a fibula 106, and a patella 108. Femur 102 includes a medial condyle 120 and tibia 104 includes a tibial plateau 122. An implant 124 in accordance with an exemplary embodiment of the present invention can be seen disposed between medial condyle 120 and tibial plateau 122 in figure 1. In some embodiments, implant 124 is substantially "kidney bean" shaped in plan view.

In the embodiment of figure 1a, implant 124 comprises a single biomaterial that itself provides first major surface 132 and second major surface 134. Second major surface 134 is positioned on tibial plateau 122 of tibia 104. First major surface 132 is shown contacting medial condyle 120 of femur 102 in figure 1a. In some advantageous embodiments of the present invention, implant 124 is substantially fixed relative to tibia 104. It will be appreciated that the implant provides a tibial projection 138 positioned and dimensioned to engage a rim 140 of tibial plateau 122. Also in the embodiment of figure 1a, a second end 142 of implant 124 is coupled to tibia 104 by a suture 144.

With continuing reference to figure 1a, it will be appreciated that femur 102 is free to rotate and/or glide relative to first major surface 132 of implant 124. In figure 1a, femur 102 is shown disposed in a first position. A second position of femur 102 is illustrated using dashed lines in figure 1a. It will be appreciated that first major surface 132 is adapted to engage medial condyle 120 of femur 102. In a typical embodiment, first major surface 132 preferably provides a femoral glide path, in the form of a surface adapted to contact and permit the articulation of the femoral condyle, to facilitate its performance. With reference to figure 1a it will be appreciated that femoral glide path 146 extends across a depression 148 in the biomaterial 126.

In the alternative embodiment of figure 1b, implant 124 comprises a first biomaterial 126 and a second biomaterial 128 that contact one another at an interface 130. With reference to figure 1b, it may be appreciated that first biomaterial 126 defines a first major surface 132 of implant 124. Similarly, second biomaterial 128 defines a second major surface 134 of implant 124. With reference to figure 1b, it may be appreciated that second major surface 134 is positioned on tibial plateau 122 of tibia 104. First major surface 132 is shown contacting medial condyle 120 of femur 102 in figure 1b.

In some advantageous embodiments of the present invention, second biomaterial 128 of implant 124 is substantially fixed relative to tibia 104. With reference to figure 1, it will be appreciated that the implant provides a tibial projection 138 positioned and dimensioned to engage a rim 140 of tibial plateau 122. Also in the embodiment of figure 1, a second end 142 of second biomaterial 128 of implant 124 is coupled to tibia 104 by a suture 144.

With continuing reference to figure 1, it will be appreciated that femur 102 is free to rotate and/or glide relative to first biomaterial 126 of implant 124. In some useful embodiments of the present invention, first major surface 132 is adapted to be positioned as an articulating surface against medial condyle 120. In figure 1, femur 102 is shown disposed in a first position. A second position of femur 102 is illustrated using dashed lines in figure 1.

With reference to figure 1, it will be appreciated that first major surface 132 is adapted to engage medial condyle 120 of femur 102. In a typical embodiment, first major surface 132 preferably provides a femoral glide path to facilitate its performance. With reference to figure 1 it will be appreciated that femoral glide path 146 extends across a depression 148 in first biomaterial 126.

Figure 2 shows various views of an implant 124 in accordance with an additional exemplary embodiment of the present invention. The views of figure 2 include a top view, a first section view taken along a section line B-B of the top view and a second section view taken along section line C-C of the top view. In the embodiment of figure 2, implant 124 comprises a first biomaterial 126 and a second biomaterial 128 that contact one another at an interface 130. In some useful

embodiments, first biomaterial 126 and a second biomaterial 128 are adhered to one another at least at interface 130.

As shown in figure 2, first biomaterial 126 defines a first major surface 132. In some useful embodiments of the present invention, first major surface 132 is adapted to be positioned against the medial condyle of a femur. For example, first major surface 132 may advantageously provide a femoral glide path in the form of a generally central depression to facilitate its performance *in situ*. In the embodiment of figure 2, first major surface 132 comprises a generally concave surface 152.

With reference to figure 2, it may be appreciated that second biomaterial 128 defines a second major surface 134 of implant 124. In some useful embodiments of the present invention, second major surface 134 of implant 124 is adapted to be positioned upon the tibial plateau of a tibia. In the embodiment of figure 2, second major surface 134 comprises a generally convex surface 154.

Figure 3 includes three additional views of implant 124 shown in the previous figure. The views of figure 3 include a bottom view, a first section view taken along a section line B-B of the bottom view and a second section view taken along section line C-C of the bottom view.

Implant 124 may be provided with features useful for securing, fixing, and/or stabilizing its position within a joint. In this instance, securing, fixing and/or stabilizing of the implant 124 within the joint generally means reducing movement of the implant 124 relative to a tibial plateau to a desired extent. As shown in figure 3, implant 124 includes a tibial projection 138 that extends beyond second major surface 134. In some useful embodiments of the present invention, tibial projection 138 is adapted to catch the posterior part of the tibial plateau by extending over the rim of the tibial plateau distally. Accordingly, fixation or stabilization of implant 124 *in situ* can be accomplished by effectively capping the tibial plateau with tibial projection 138 extending distally over the rim of the plateau at one end of implant 124 and by attaching another end of implant 124 with sutures or additional projections. Implant 124 of figure 3 defines a hole 156. In some embodiments of the present invention, hole 156 is dimensioned so as to allow one or more sutures to pass therethrough.

Implant 124 of figure 3 comprises a first biomaterial 126 and a second biomaterial 128. In some cases first biomaterial 126 may have a first wear resistance, congruence, and cushioning (shock attenuation), while second biomaterial 128 has a second wear resistance, congruence, and cushioning. In some cases, second biomaterial 128 may comprise a material selected to provide a relatively high level of congruence and cushioning and first biomaterial 126 may comprise a material selected to provide a high level of wear resistance. When this is the case, the first congruence and cushioning may be greater than the second congruence and cushioning, while the second wear resistance is greater than the first wear resistance. Various methods may be used to assess the wear resistance and shock attenuating properties of materials without deviating from the spirit and scope of the present invention.

In some cases first biomaterial 126 may have a first congruence and cushioning and a first abrasion resistance, while second biomaterial 128 has a second congruence and cushioning and a second abrasion resistance. In some cases, second biomaterial 128 may comprise a material selected to provide a relatively high level of congruence and cushioning and first biomaterial 126 may comprise a material selected to provide a high level of abrasion resistance. When this is the case, the first congruence and cushioning may be greater than the second congruence and cushioning, while the second abrasion resistance is greater than the first abrasion resistance. Various methods may be used to assess the abrasion resistance of materials without deviating from the spirit and scope of the present invention.

In some embodiments of the present invention, one part of implant 124 comprises a metallic material, and the other part of implant 124 comprises a non-metallic material. In some embodiments, the implant 124 may comprise a combination of materials to provide for desired characteristics.

Figure 4 includes various views of a first biomaterial 326 that may form a portion of an implant in accordance with an additional exemplary embodiment of the present invention. First biomaterial 326 comprises a first member 358 and a second member 360. In the embodiment of figure 4, first member 358 and second member 360 are joined at a weld joint 362. It is to be appreciated, however, that embodiments

of the present invention are possible in which first member 358 and second member 360 are formed from a single piece of material. A first member and a second member can be formed in one piece using, for example, a casting or molding process. With reference to figure 4, it will be appreciated that first member 358 and second member 360 define a chamber 365. In the embodiment of figure 4, first member 358 defines a plurality of apertures 366 communicating with chamber 365.

Figure 5 is a cross-sectional view of a mold 368 in accordance with an exemplary embodiment of the present invention. Mold 368 comprises a first tool 370 and a second tool 372. As shown in figure 5, first tool 370 and second tool 372 define a cavity 364. In the embodiment of figure 5, a first biomaterial 326 is disposed within cavity 364. The mold is optionally, and preferably, heated in order to facilitate the curing process, and is also optionally, and preferably, provided with a release coating in the manner described herein.

Figure 6 is an additional cross-sectional view of mold 368 shown in the previous figure. In the embodiment of figure 6, an implant 324 comprising first biomaterial 326 and a second biomaterial 328 is disposed within cavity 364 defined by first tool 370 and second tool 372. In some methods in accordance with the present invention, a second material 374 is injected into cavity 364 to form second biomaterial 328.

Figure 7 shows various views of implant 324 shown in the previous figure. With reference to figure 7, it will be appreciated that implant 324 comprises a first biomaterial 326 and a second biomaterial 328. In the embodiment of figure 7, first biomaterial 326 and second biomaterial 328 contact one another at an interface 330. In some useful embodiments of the present invention, first biomaterial 326 and second biomaterial 328 are adhered to one another at least at interface 330. In some embodiments, first biomaterial 326 and second biomaterial 328 are molded and cured together, creating a monolithic implant with superior strength (e.g., tear strength) properties. In some embodiments, the strength of the interface is greater than the strength of the surrounding materials to prevent delamination.

With reference to figure 7, it will be appreciated that first biomaterial 326 and second biomaterial 328 may also be also mechanically interlocked with one another. As shown in figure 7, second biomaterial 328 includes a plurality of protrusions 376 that extend through apertures 366 defined by first biomaterial 326. In the embodiment of figure 7, a first portion 378 of second biomaterial 328 is disposed on a first side 380 of first member 358 and a second portion 382 of second biomaterial 328 is disposed on a second side 384 of first member 358.

Figure 8 includes various additional views of implant 324 shown in the previous figure. The views shown in figure 8 include a top view, a first section view taken along a section line B-B of the top view and a second section view taken along section line C-C of the top view. With reference to figure 8, it will be appreciated that implant 324 includes a relief 386. In some useful embodiments of the present invention, relief 386 is dimensioned to receive the intercondylar eminence (ICE) of a human tibia. In the embodiment of figure 8, first biomaterial 326 of implant 324 comprises a mesial ridge 390. In some useful embodiments of the present invention, mesial ridge 390 is positioned and dimensioned so as to extend between the femoral medial condyle and the intercondylar eminence (ICE) of a tibia when implant 324 is implanted in a human body.

Figure 9 is a perspective view of a first biomaterial 426 that may form a portion of an implant in accordance with an additional exemplary embodiment of the present invention. With reference to figure 9, it will be appreciated that first biomaterial 426 defines a first recess 492 and a second recess 494. In the embodiment of figure 9, each recess comprises a slot 498 having a neck portion 200 and a bottom portion 202. In the embodiment of figure 9, the lateral cross-section of each slot has a generally dovetail-like shape in lateral cross-section.

Figure 10 includes various views showing a first biomaterial 526 that may form a portion of an implant in accordance with an additional exemplary embodiment of the present invention. First biomaterial 526 of figure 10, defines a first recess 592, a second recess 594, and a third recess 596. Each recess comprises a slot 598 having a neck portion 200 and a bottom portion 202 in the embodiment of figure 10. As illustrated in figure 10, neck portion 200 of each slot 598 has a first dimension 204

and bottom portion 202 of each slot 598 has a second dimension 206. In the embodiment of figure 10, second dimension 206 is generally larger than first dimension 204.

Figure 11 shows various views of an implant 524 including first biomaterial 526 shown in the previous figure. With reference to figure 11, it will be appreciated that implant 524 also includes a second biomaterial 528 comprising a second material 574. Second biomaterial 528 of implant 524 may be formed, for example, by placing first biomaterial 526 into a mold cavity and injection second material 574 into the mold cavity.

In the embodiment of figure 11, first biomaterial 526 contacts second biomaterial 528 at an interface 530. In some useful embodiments of the present invention, first biomaterial 526 and second biomaterial 528 are adhered to one another, optionally by an adhesive, at least at an interface 530. Such an adhesive may be used regardless of whether the implant is formed in a heated mold, as discussed below. With reference to figure 11, it will be appreciated that first biomaterial 526 and second biomaterial 528 are also mechanically interlocked with one another.

As shown in figure 11, second biomaterial 528 includes a plurality of protrusions 208 that extend beyond interface 530. In the embodiment of figure 5, each protrusion 208 of second biomaterial 528 extends into a recess 220 of first biomaterial 526. In the embodiment of figure 11, first protrusion 208 has dimensions that are similar to those of each recess 220. With reference to figure 11 it will be appreciated that each protrusion 208 includes an enlarged portion 222. In the embodiment of figure 11, a body 224 of second biomaterial 528 is disposed on a first side 580 of interface 530 and enlarged portion 222 of each protrusion 208 is disposed on a second side 584 of interface 530. With reference to figure 11, it will be appreciated that each recess 220 and each protrusion 208 is shaped so as to provide mechanically interlocking engagement between first biomaterial 526 and second biomaterial 528 of implant 524.

Figure 12 includes various additional views of implant 524 shown in the previous figure. The views shown in figure 12 include a top view, a first section view taken along a section line B-B of the top view and a second section view taken along section line C-C of the top view. With reference to figure 12, it will be appreciated

that implant 524 includes a relief 586. In some useful embodiments of the present invention, relief 586 is dimensioned to receive the intercondylar eminence (ICE) of a human tibia. In the embodiment of figure 12, first biomaterial 526 of implant 524 comprises a mesial ridge 590. In some useful embodiments of the present invention, mesial ridge 590 is positioned and dimensioned so as to extend between the medial condyle a femur and the intercondylar eminence (ICE) of a tibia when implant 524 is implanted in the body.

Figure 13 is a partial front view of a human skeleton including a left leg 226 and a right leg 600. Left leg 226 includes a left femur 602, a left tibia 604 and a left fibula 606. Similarly, right leg 600 includes a right femur 602, a right tibia 604 and a right fibula 606. The patella, or knee cap, is not shown in figure 13. Each femur includes a medial condyle 620 and a lateral condyle 232. Each tibia includes a tibial plateau 622. In figure 13, it may be appreciated that a left implant 624 in accordance with the present invention, is interposed between the medial condyle 620 of left femur 602 and the tibial plateau 622 of left tibia 604. Similarly, a right implant 624 in accordance with the present invention is interposed between the medial condyle 620 of right femur 602 and the tibial plateau 622 of right tibia 604.

In the embodiment of figure 13, each implant comprises a first biomaterial 626 and a second biomaterial 628. With reference to figure 13, it may be appreciated that first biomaterial 626 of each implant includes a mesial ridge 690. In figure 13, the mesial ridge 690 of each implant is shown extending between the medial condyle 620 a femur and the intercondylar eminence (ICE) 688 of a tibia.

Figure 14 is a top view showing a left tibia 704 and right tibia 705. In the embodiment of figure 14, a right implant 725 is disposed on a tibial plateau 722 of right tibia 705. With reference to figure 14, it will be appreciated that right implant 725 includes a relief 786 that is dimensioned to receive the intercondylar eminence (ICE) 788 of right tibia 705. Also in the embodiment of figure 14, a left implant 724 is disposed on a tibial plateau 722 of left tibia 704. Left implant 724 includes a relief 786 that is dimensioned to receive the intercondylar eminence (ICE) 788 of left tibia 704 in the embodiment of figure 14.

Figure 15 shows various views of a preformed knee implant (810) prepared using an ex vivo mold according to the present invention. The implant provides a first major surface (812) adapted to be positioned upon the tibial surface, and a second major surface (814) adapted to be positioned against the femoral condyle. In a typical embodiment, the second major surface, in turn, is preferably provided with a femoral glide path (816) to facilitate its performance *in situ*, in the form of a generally central (e.g., oval) depression about 0.5 mm, or more preferably about 1 mm to about 5 mm deep at its lowest point (2 mm as shown) and about 20 mm, and more preferably about 30 mm to about 50 mm in length by 10 mm to 30 mm in width (40 mm by 20 mm as shown). Those skilled in the art, given the present description, will readily determine the actual dimensions for optimal use, in both absolute and relative terms, depending on such factors as the actual joint size and desired results (e.g., angular correction). As shown, the implant is also provided with a tibial projection (818), adapted to catch the posterior portion of the tibial plateau by extending over the rim of the tibial plateau distally. The body of the implant can have dimensions on the order of between about 35 mm, and preferably about 40 mm to about 60 mm in the anterior-posterior dimension, between about 20 mm, and preferably 30 mm to about 35 mm, or even about 40 mm in the medial-lateral dimension, and a maximum thickness (at the posterior lip of between about 8 mm, more preferably about 10 mm, and about 20 mm, or about 2 mm to about 4 mm (e.g., 3 mm) greater than the thickness of the implant at the center. As a result, it can be seen that fixation is accomplished by effectively capping the tibial plateau with one or more projections extending distally over the rim of the plateau.

Figure 16 shows various views of an implant in accordance with an exemplary embodiment of the present invention. In figure 16, a distance A is shown extending from the most anterior point of the implant to the upper inner radius of the posterior lip of the implant. A distance B is also illustrated in figure 16. Distance B may be described as the height of the posterior lip. Distances C, D, and E are also illustrated in figure 16.

The dimensions of the implant may be scaled to fit a particular size of patient. In one exemplary embodiment of the present invention, distance A is about 54.0 mm, distance B is about 5.6 mm, distance C is about 7.0 mm, distance D is about 29.2 mm, and distance E is about 2.1 mm.

In some advantageous embodiments of the present invention, distance A is, for example, between about 30 mm and about 60 mm.

In some advantageous embodiments of the present invention, distance B is, for example, between about 1 mm and about 10 mm.

In some advantageous embodiments of the present invention, distance C is, for example, between about 1 mm and about 10 mm.

In some advantageous embodiments of the present invention, distance D is, for example, between about 10 mm and about 40 mm.

In some advantageous embodiments of the present invention, distance E is, for example, between about 0.2 mm and about 4 mm.

Implants such as those described above are preferably used in a method that includes first determining the proper implant thickness needed to match physiological valgus. The surgeon prepares the site arthroscopically, removing excess cartilage and removing the medial meniscus to the medial rim, using a portal of about 1 cm in order to provide suitable arthroscopic access while maintaining the presence of fluid in the joint.

An implant of the type shown herein provides various benefits, including the correction of various deformities, based in significant part upon the presence and configuration of the mesial lip and the cutout (kidney bean shaped) for the intercondylar eminence. The tibial projection is adapted to catch the posterior part of the tibial plateau. The implant itself has dimensions as provided herein, and can be provided using one of a collection of molds of multiple sizes and/or styles in accordance with the various parameters of the present invention. A kit may be supplied for providing implants of various sizes (e.g., implants having thicknesses varying by 1 mm or 2 mm increments and implants having a range of anterior to posterior dimensions). Implants having different shapes may also be provided (e.g., implants shaped for the left knee and implants shaped for the right knee).

In some embodiments, a range of implant sizes can be provided and sizing can be accomplished by physical measurement (e.g., an AP length) using tools and methods as described in International Publication Number WO 2004/006811 A2, the contents of which are herein incorporated by reference. Such an embodiment may include the steps of preparing a joint to receive an implant, including the preparation or resurfacing of a femoral condyle and/or a tibial plateau, determining an appropriate implant size for a particular joint, determining an appropriate implant thickness needed to match physiological values, and inserting the implant into the joint, as well as the related components and/or devices for performing each step. In such an embodiment, multiple sizes can be made off site and the selection of the appropriate implant size can be chosen at the time of surgery. Alternatively, the pre-made material can be made off site to specifications developed from imaging of the patient's joint surface.

In some embodiments, the surgeon may prepare the site arthroscopically, removing excess cartilage while preserving the medial collateral ligament and meniscal rim to the extent possible, using a portal of about 1cm in order to provide suitable arthroscopic access while maintaining the presence of fluid in the joint. The implant can be initially molded ex vivo, including as either a manufactured part or at the time of use, using a mold selected from those available and including one or more embedded or attached fixation parts (e.g., anterior sutures or tabs), at which time it is inserted into the knee and within the remaining parts. The surgeon will then typically feel the implant once in position, to confirm that the implant is properly seated, and will extend the knee to provide varus stress on the lower leg, optionally obtaining congruency as the implant continues to cure by finally molding both surfaces of the implant (to both the tibial surface and condyle, respectively).

Optionally, and preferably, the surgeon can also use a femoral forming device (e.g., spoon-shaped device) of the type described in Applicant's copending PCT application No. PCT/US02/40883, publication No. WO 03/053278, the disclosure of which is incorporated herein by reference, in order to prepare a femoral condyle surface for better congruency with a tibial plateau, and to remove unwanted undulations.

The implant can be sutured to the anterior rim, and the knee can be flexed to obtain complete range of motion. Optionally, during or following this procedure, the joint can be filled with a suitable fluid and visualized, the joint space irrigated and all debris removed, after which the knee is extended and braced, with the access portal(s) closed by suitable means (e.g., sutured).

In some embodiments, the invention comprises a hip implant 1000, as shown in Figure 17. Normally, a hip functions through a wide range of motion and supports loads several times an individual's body weight. Articular cartilage on both surfaces of the hip joint aid in absorbing impact, distributing load, maintaining alignment and minimizing friction. In patients with osteoarthritis, the articular cartilage may be thinned or completely eliminated, resulting in pain that may become disabling. The current treatment for certain painful osteoarthritis of the hip is total hip replacement. This procedure involves removal of the femoral head and the insertion of a metal stem into the shaft of the femur. The stem is usually capped with a Morris Taper junction metallic ball. On the acetabular side of the joint, a metal cup lined with Ultra High Molecular Weight Polyethelene (UHMWPE) is inserted into the pelvic bone. The cup and stem are usually affixed with a Polymethyl Methacrolate (PMMA) grout or may have a bone in-growth fixation.

In some embodiments, the present invention comprises an interpositional polymeric hip implant 1000 positioned in the acetabulum to provide a wear and load bearing surface in an arthritic hip joint. Such an implant can be placed by minimally invasive surgical techniques or with a larger exposure. The implant may be provided in multiple sizes.

The hip implant 1000 may comprise one material or may be divided into one or more sections, and different sections may comprise different materials. In some embodiments, the major load bearing area 1010 of the implant is composed of a high durometer, wear resistant polyurethane and the remaining half 1020 is composed of a softer durometer, more compliant polyurethane. In such embodiments, the compliant portion of the implant may allow it to be folded for insertion as shown in Figure 18, and thereby inserted through a minimally invasive surgical incision (i.e., 4 cm). In some embodiments, the implant may cover the femoral head with the harder modulus

on the superior weight bearing surface and the softer more elastomeric material around the junction with the femoral neck.

The implant 1000 may be retained within the hip joint by any suitable method. In some embodiments, the implant 1000 has a configuration resembling the acetabulum to fit between the acetabulum and the femoral head, and can have an opening or depression to accommodate the ligament of the head of the femur. Further, the implant may be shaped to be congruent with the major anatomical features of the acetabulum. In some embodiments, hip implant 1000 may have a series of anchors (e.g., 1-5) of barbed polyurethane to insert into predrilled holes and press-fit into the acetabulum. In embodiments so provided, the softer durometer material portion may have an enlargement on the acetabular surface that fits into the fovea and provides added rotational stability to the implant. The implant 1000 may also have tabs or fabric around the rim to provide for suture fixation or tissue in-growth to enhance stability.

In some embodiments, an insertion tool 1050 may be used to place the implant 1000 within the hip, as shown in Figure 19. Such an insertion tool 1050 is useful for allowing placement of the implant 1000 through a relatively small incision. In some embodiments, the insertion tool 1050 may include double tongs 1060 and a single tong 1070. In use for deployment in some embodiments, the double tongs 1060 may straddle the low modulus portion 1020 of the implant 1000 when the implant is in a closed position as shown in Figure 18. The single tong 1070 may be placed at the apex of the high modulus portion. After insertion into the hip joint, the insertion tool 1070 may be opened to unfold the implant 1000.

The invention may also include other instruments useful for the preparation of the joint or placement of the implant. In some embodiments, the invention includes a joint preparing tool 1100, as shown in Figures 20(a)-(c). Joint preparing tool 1100 may comprise a head portion 1110 and a handle portion 1120. Head portion 1110 may be provided with any suitable feature such as rasps, grooves, or fenestrations to smooth and/or remove undesirable debris from the joint site before insertion of the implant. In some embodiments, the head 1110 is provided with a cup-type shape to facilitate smoothing of the acetabular and/or femur head. Instruments 1050 and 1100 may be provided in a set of instruments, with or without the implant, that allows the

surgeon to prepare the acetabulum and femoral head through the arthroscopic portals or the mini-incision for placement of the acetabular implant.

Such an implant can be placed by minimally invasive surgical techniques or with a larger exposure. In some embodiments, an incision is made proximate the hip and the joint is prepared to receive the implant, such as by smoothing the surface of the acetabulum and/or femur head. This smoothing step may be performed using a tool such as described above. The implant may be provided in multiple sizes, and trial implant may be used to accurately gauge the preferred implant size for a particular patient. The implant may then be placed into the joint by any suitable method, such as the method described above. The implant may be inserted and deployed with or without dislocating the hip. In some embodiments, an external distracter may be used to provide acceptable joint space. After proper placement of the implant and fit confirmation, the incision may be closed.

In some embodiments, the invention includes a knee spacer (e.g., shim) 1200, as shown in Figures 21(a)-(f). Polymeric knee spacer 1200 may be comprised of any of the biomaterials discussed above or below, and is useful for correcting and/or adapting various sizes and angles of a total knee replacement, such as a temporary total knee replacement. In some embodiments, spacer 1200 may be between about 0.6 inches and 1.0 inches wide. In the embodiments shown in Figures 21(a)-(f), one or more spacers is shown in apposition to femoral component 1220 and/or tibial component 1240. Femoral component 1220 may be anchored to a femur via a femoral component modular stem 1250, and tibial component 1240 may be anchored to a tibia via a tibial component modular stem 1260. Femoral component 1220 and tibial component 1240 may each have one or more recesses 1270, useful for receiving and/or retaining spacer 1200. In some embodiments, spacer 1200 contains one or more drugs, as discussed further below.

The implantable material for use in resurfacing a joint can be formed *ex vivo* as an injectable material that sets up to the molded shape. Various methods for changing the state of a composition from liquid to a suitable solid include a suitable combination of heating (or cooling) time, and chemical reactivity. A chemical reaction can be exothermic or endothermic, and can be initiated in any suitable manner, e.g., activated by light and/or heat, or chemically catalyzed. Examples of

such systems include flowable polymers of two or more components, light activated polymers, and polymers cured either by the use of catalysts or by heat, including body heat, or any suitable combination thereof. As a further embodiment, the material can be synthesized *ex vivo* and then machined to fit, using imaging and/or to a predetermined geometry and size of the implant.

Fixation methods for the implant may include biologic glues to glue the implant to the underlying surface, trapping of the implant into a cavity on the surface that causes a mechanical lock, using various anchors to the underlying structure and fixing the implant to that surface or using mold retainers and/or screws, staples, sutures or pins. In alternative embodiment, anchors in the underlying structure may be used for fixing the implant to that surface and the implant can be adapted to permit or encourage the growth of tissue thereon, and/or by encapsulation, to secure anchoring.

In a preferred method of use, the patient will have a diagnosis of osteoarthritis and have loss of cartilage on the articulating surface. A determination will be made of the amount of correction needed for the reestablishment of a normal angle of articulation. The ligaments will be balanced so that there is no loss of range of motion with the implant in place and the surface will be placed in such a position that the eventual resulting surface geometry reestablishes the same plane and orientation of the original articular surface. Patients with cartilage loss due to inflammatory arthritis may also be treated in this way.

Access to the site is obtained in a minimally invasive way. In a preferred embodiment, this is accomplished through arthroscopic means with arthroscopic portals. In an alternative embodiment, the access is accomplished by a mini arthrotomy with a small incision that allows access to the joint without sacrificing nerves, vessels, muscles or ligaments surrounding the joint. In the preferred embodiment fibrillated articulating cartilage that is degenerated is removed down to the subchondral surface. In one such embodiment, the surface can be dried and prepared for appropriate anchoring, including by the preparation and use of anchor points within the joint surface, to provide a mechanical lock and/or to simply provide horizontal and lateral stability. The surface may be prepared by drying and roughening in case a tissue adhesive is used. Pre-made anchors may be installed.

These may be made of various metallic materials or of polymers and may consist of pegs that would extend up through the implant to anchor it to the underlying surface. This surrounding subchondral bone may be roughened to enhance tissue growth on to the implant, as well as implant adhesion.

Two alternatives shown in Figure 2 of the parent provisional application include a single segment that can be installed through a portal or a series of segments that can be installed through a portal and locked together once inside the joint. They would be placed sequentially and then anchored to the bone by anchor points cut in the bone or by screws or tissue growth onto and/or around the implant. Finally, a robot, jig or other cutting template/fixture can be used to prepare the bony surface for the pre-made implant to a fixed geometry of the anchor point. A multi-segmented implant of this invention preferably does not require anchoring or fixing to the bony surface; and instead can be stabilized by shape and/or designed in a manner similar to a fully *ex vivo* molded implant.

Both the preformed component(s) and flowable biomaterial, if used, can be prepared from any suitable material. Generally, a material is suitable if it has appropriate biostability, biodurability and biocompatibility characteristics. Typically, the materials include polymeric materials, having an optimal combination of such properties as biostability, biodurability, biocompatibility, physical strength and durability, and compatibility with other components (and/or biomaterials) used in the assembly of a final composite.

Examples of polymeric materials that may be suitable in some applications, either alone or in combination, include polyurethane, available from Polymer Technology Group Incorporated under the names Bionate,™ Biospan,™ and Elasthane™, available from Dow Chemical Company under the name Pellethane,™ and available from Bayer Corp. under the names Bayflex,™ Texin,™ and Desmopan;™ ABS, available from GE Plastics under the name Cycolac™, and available from Dow Chemical Company under the name Magnum;™ SAN, available from Bayer Plastics under the name Lustran;™ Acetal, available from Dupont under the name Delrin,™ and available from Ticona GmbH and/or Ticona LLC (Ticona) under the name Celcon;™ polycarbonate, available from GE Plastics under the name Lexan,™ and available from Bayer Corp. under the name Makrolon;™ polyethylene, available from Huntsman LLC, and available from Ticona under the names

GUR 1020™ and GUR 1050;™ polypropylenes, available from Solvay Engineered Polymers, Inc. under the name Dexflex;™ aromatic polyesters, available from Ticona; polyetherimide (PEI), and available from GE Plastics under the name Ultem;™ polyamide-imide (PAI), available from DSM E Products under the name Torlon;™ polyphenylene sulfide, available from Chevron Phillips Chemical Company LP under the name Ryton;™ polyester, available from Dupont under the name Dacron;™ polyester thermoset, available from Ashland Specialty Chemical Company under the name Aropol;™ polyureas; hydrogels, available from Hydromer Inc.; liquid crystal polymer, available from Ticona under the name Vectra;™ polysiloxanes, available from Nusil Technologies, Inc.; polyacrylates, available from Rohm & Haas under the name Plexiglas;™ epoxies, available from Ciba Specialty Chemicals; polyimides, available from Dupont under the names Kapton,™ and Vespel;™ polysulfones, available from BP Amoco Chemicals under the name Udel,™ and available from BASF Corporation under the name Ultrason;™ PEAK/PEEK, available from Victrex under the name Victrex PEAK;™ as well as biopolymers, such as collagen or collagen-based materials, chitosan and similar polysaccharides, and combinations thereof. Of course, any of the materials suitable for use in a composite or single biomaterial implant may be structurally enhanced with fillers, fibers, meshes or other structurally enhancing means.

The present invention provides a biomaterial having an improved combination of properties for the preparation, storage, implantation and long term use of medical implants. The improved properties correspond well for the preparation and use of an implant having both weight bearing and/or articulating functions, and preferably in the form of an implant for interpositional arthroplasty.

In turn, a preferred biomaterial of this invention provides an optimal combination of properties relating to wear resistance, congruence, and cushioning while meeting or exceeding requirements for biocompatibility, all in a manner that serves to reduce the coefficient of friction at the major motion interface.

Wear resistance can be assessed by determining parameters such as DIN abrasion and flexural stress strain fatigue resistance. A preferred implant will have sufficient wear resistance to avoid the generation of clinically significant particulate debris over the course of the implant's use.

Congruence can be assessed by determining parameters such as tensile modulus compressive modulus, and hardness, to determine the manner and extent to which the implant will conform itself to possible other components of the implant itself and/or to bone or surrounding tissue.

Cushioning can be assessed by determining such parameters as hardness, compressive modulus, and tensile modulus, to determine the elastomeric nature of the material, and in turn, its suitability for use in a weight bearing joint. More elastomeric materials will generally provide greater comfort in weight bearing applications, particularly if the other physical properties can be maintained.

Applicant has discovered that improved wear resistance, congruence, and/or cushioning toughness can be achieved without undue effect on other desired properties, such as abrasion, hardness, specific gravity, tear resistance, tensile strength, ultimate elongation, and biocompatibility. Moreover, Applicant has discovered that such properties can themselves be provided in varying forms, as between first and second biomaterials of a composite of the present invention.

A polymeric biomaterial of this invention can be prepared using any suitable means, including by curing the polymer ex vivo. The composition can be used in any suitable combination with other materials, including other compositions of the same or similar nature, as well as other materials such as natural or synthetic polymers, metals, ceramics, and the like.

The invention further provides a method of preparing the composition, a method of using the composition, implants that comprise the composition, as well as methods of preparing and using such implants.

The biomaterial used in this invention preferably includes polyurethane components that are reacted *ex vivo* to form a polyurethane ("PU"). The formed PU, in turn, includes both hard and soft segments. The hard segments are typically comprised of stiffer oligourethane units formed from diisocyanate and chain extender, while the soft segments are typically comprised of one or more flexible polyol units. These two types of segments will generally phase separate to form hard and soft segment domains, since they tend to be incompatible with one another. Those skilled in the relevant art, given the present teaching, will appreciate the manner in which the relative amounts of the hard and soft segments in the formed polyurethane, as well as

the degree of phase segregation, can have a significant impact on the final physical and mechanical properties of the polymer. Those skilled in the art will, in turn, appreciate the manner in which such polymer compositions can be manipulated to produce cured and curing polymers with desired combination of properties within the scope of this invention.

The hard segments of the polymer can be formed by a reaction between the diisocyanate or multifunctional isocyanate and chain extender. Some examples of suitable isocyanates for preparation of the hard segment of this invention include aromatic diisocyanates and their polymeric form or mixtures of isomers or combinations thereof, such as toluene diisocyanates, naphthalene diisocyanates, phenylene diisocyanates, xylylene diisocyanates, and diphenylmethane diisocyanates, and other aromatic polyisocyanates known in the art. Other examples of suitable polyisocyanates for preparation of the hard segment of this invention include aliphatic and cycloaliphatic isocyanates and their polymers or mixtures or combinations thereof, such as cyclohexane diisocyanates, cyclohexyl-bis methylene diisocyanates, isophorone diisocyanates and hexamethylene diisocyanates and other aliphatic polyisocyanates. Combinations of aromatic and aliphatic or arylakyl diisocyanates can also be used.

The isocyanate component can be provided in any suitable form, examples of which include 2,4'-diphenylmethane diisocyanate, 4,4'-diphenylmethane diisocyanate, and mixtures or combinations of these isomers, optionally together with small quantities of 2,2'-diphenylmethane diisocyanate (typical of commercially available diphenylmethane diisocyanates). Other examples include aromatic polyisocyanates and their mixtures or combinations, such as are derived from phosgenation of the condensation product of aniline and formaldehyde. It is suitable to use an isocyanate that has low volatility, such as diphenylmethane diisocyanate, rather than more volatile materials such as toluene diisocyanate. An example of a particularly suitable isocyanate component is the 4,4'-diphenylmethane diisocyanate ("MDI"). Alternatively, it can be provided in liquid form as a combination of 2,2'-, 2,4'- and 4,4'- isomers of MDI. In a preferred embodiment, the isocyanate is MDI and even more preferably 4,4'-diphenylmethane diisocyanate.

In one embodiment of the invention, the isocyanate is 4,4'-diphenylmethane diisocyanate (as available from Bayer under the tradename Mondur M), from preferably about 20 to 60 weight percent, more preferably from about 30 to 50 weight percent. The actual amount of isocyanate used should be considered in combination with other ingredients and processing parameters, particularly including the amount of chain extender (such as butanediol (BDO)) used, since the combination typically determines the hard segment component, and in turn hardness, of the corresponding cured polymer. Hardness correlates in a generally proportional fashion with the combined weights of MDI and BDO, such that compositions having between 30 and 60 total weight percent (MDI + BDO) are generally useful, with those compositions having between about 50 to about 60 total weight percent being somewhat harder, and particularly useful for either the first (femoral contacting) biomaterial and surface of a composite implant or for implants having a single biomaterial providing both first and second surfaces. By contrast, compositions having between about 40 to about 50 total weight percent are somewhat more congruent and cushioning, though less wear resistant, and therefore are preferred for use as the second biomaterial, e.g., tibial contacting surface, of a composite implant as described herein.

Some examples of chain extenders for preparation of the hard segment of this invention include, but are not limited, to short chain diols or triols and their mixtures or combinations thereof, such as 1,4-butane diol, 2-methyl-1,3-propane diol, 1,3-propane-diol ethylene glycol, diethylene glycol, glycerol, tri-methylpropane, cyclohexane dimethanol, triethanol amine, and methyldiethanol amine. Other examples of chain extenders for preparation of the hard segment of this invention include, but are not limited to, short chain diamines and their mixtures or combinations thereof, such as dianiline, toluene diamine, cyclohexyl diamine, and other short chain diamines known in the art.

The soft segment consists of urethane terminated polyol moieties, which are formed by a reaction between the polyisocyanate or diisocyanate or polymeric diisocyanate and polyol. Examples of suitable diisocyanates are denoted above. Some examples of polyols for preparation of the soft segment of this invention include but are not limited to polyalkylene oxide ethers derived form the condensation

of alkylene oxides (e.g. ethylene oxide, propylene oxide, and blends thereof), as well as tetrahyrofuran based polytetramethylene ether glycols, polycaprolactone diols, polycarbonate diols and polyester diols and combinations thereof. In a preferred embodiment, the polyols are polytetrahydrofuran polyols ("PTHF"), also known as polytetramethylene oxide ("PTMO") or polytetramethylene ether glycols ("PTMEG"). Even more preferably, the use of two or more of PTMO diols with different molecular weights selected from the commercially available group consisting of 250, 650,1000, 1400, 1800, 2000 and 2900.

Two or more PTMO diols of different molecular weight can be used as a blend or separately, and in an independent fashion as between the different parts of a two part system. The solidification temperature(s) of PTMO diols is generally proportional to their molecular weights. The compatibility of the PTMO diols with such chain extenders as 1,4-butanediol is generally in the reverse proportion to the molecular weight of the diol(s). Therefore the incorporation of the low molecular weight PTMO diols in a "curative" (part B) component of a two part system, and higher molecular weight PTMO diols in the prepolymer (part A) component, can provide a two-part system that can be used at relatively low temperature. In turn, good compatibility of the low molecular weight PTMO diols with such chain extenders as 1,4-butanediol permits the preparation of two part systems with higher (prepolymer to curative) volume ratio. Amine terminated polyethers and/or polycarbonate-based diols can also be used for building of the soft segment.

In one embodiment of the invention, the polyol is polytetramethyleneetherglycol 1000 (as available from E.I. du Pont de Nemours and Co. under the tradename Terathane 1000), preferably from about 0 to 40 weight percent, more preferably from about 10 to 30 weight percent, and perhaps even more preferably from about 22 to 24 weight percent, based on the total weight of the polymer. The polyol disclosed above may be used in combination with polytetramethyleneetherglycol 2000 (as available from E.I. du Pont de Nemours and Co. under the tradename Terathane 2000), preferably from about 0 to 40 weight percent, more preferably from about 10 to 30 weight percent, and perhaps even more preferably from about 17 to 18 weight percent, based on the total weight of the polymer.

In one embodiment, the biomaterial may include a chain extender. For example, the chain extender may be 1,4-butanediol (as available from Sigma Aldrich Corp.), preferably from about 1 to 20 weight percent, more preferably from 5 to 15 weight percent, to perhaps even more preferably from 12 to 13 weight percent, based on the total weight of the polymer.

The polyurethane can be chemically crosslinked, e.g., by the addition of multifunctional or branched OH-terminated crosslinking agents or chain extenders, or multifunctional isocyanates. Some examples of suitable crosslinking agents include, but are not limited to, trimethylol propane ("TMP"), glycerol, hydroxyl terminated polybutadienes, hydroxyl terminated polybutadienes (HOPB), trimer alcohols, Castor oil polyethyleneoxide (PEO), polypropyleneoxide (PPO) and PEO-PPO triols. In a preferred embodiment, HOPB is used as the crosslinking agent.

This chemical crosslinking augments the physical or "virtual" crosslinking of the polymer by hard segment domains that are in the glassy state at the temperature of the application. The optimal level of chemical cross-linking improves the compression set of the material, reduces the amount of the extractable components, and improves the biodurability of the PU. This can be particularly useful in relatively soft polyurethanes, such as those suitable for the repair of damaged cartilage. Reinforcement by virtual cross-links alone may not generate sufficient strength for *in vivo* performance in certain applications. Additional cross-linking from the soft segment, potentially generated by the use of higher functional polyols can be used to provide stiffer and less elastomeric materials. In this manner a balancing of hard and soft segments, and their relative contributions to overall properties can be achieved.

In one embodiment, the chemical cross-linking agent is 2-ethyl-2-(hydroxymethyl)-1,3-propanediol (also known as trimethylolpropane, as available from Sigma Aldrich Corp.), preferably from about 0 to 5 weight percent, more preferably from about 0.1 to 1 weight percent, and perhaps even more preferably from about 0.15 to 0.3 weight percent, based on the total weight of the polymer.

Additionally, and optionally, a polymer system of the present invention may contain at least one or more biocompatible catalysts that can assist in controlling the curing process, including the following periods: (1) the cure induction period, and (2)

the full curing period of the biomaterial. Together these two periods, including their absolute and relative lengths, and the rate of acceleration or cure within each period, determine the cure kinetics or profile for the composition. In some embodiments, however, a catalyst is not included. For instance embodiments in which the biomaterial is heated in the course of curing, such as in a heated mold in the manner described herein, can performed without the use of a catalyst.

Some examples of suitable catalysts for preparation of the formed PU of this invention include, but are not limited to, tin and tertiary amine compounds or combinations thereof such as dibutyl tin dilaurate (DBTDL), and tin or mixed tin catalysts including those available under the tradenames "Cotin 222", "Fomrez UL-22" (Crompton Corp.), "dabco" (a triethylene diamine from Sigma-Aldrich), stannous octanoate, trimethyl amine, and triethyl amine.

In one embodiment of the invention, the catalyst is bis-(dodecylthio)-dimethylstannane (available from Crompton Corp. as Fomrez catalyst UL-22), preferably from about 0 to 2 weight percent, more preferably from about 0 to 1 weight percent, and perhaps most preferably from 0.0009 to 0.002 weight percent, based on the total weight of the polymer.

Further, a polymer stabilizer additive useful for protecting the polymer from oxidation may be included. In one embodiment of the invention, the additive is pentaerythritol tetrakis (3-(3,5-di-tert-buyl-4-hydroxyphenyl)proprionate (available from Ciba Specialty Chemicals, Inc. as Irganox 1010), preferably from about 0 to 5 weight percent, more preferably about 0.1 to 1 weight percent, and perhaps even more preferably about 0.35 to 0.5 weight percent, based on the total weight of the polymer.

Optionally, other ingredients or additives can be included, for instance, a reactive polymer additive can be included from the group consisting of hydroxyl- or amine-terminated compounds selected from the group consisting of poybutadiene, polyisoprene, polyisobutylene, silicones, polyethylene-propylenediene, copolymers of butadiene with acryolnitrile, copolymers of butadiene with styrene, copolymers of isoprene with acrylonitrile, copolymers of isoprene with styrene, and mixtures of the above. Other additives may also be optionally provided. For example, catalysts such as Dabco, antioxidants such as vitamin E, hydrophobic additives such as hydroxyl-

terminated polybutadiene, and dye green GLS, singularly or in combination, may be included in the polymer formulation.

In some embodiments of the invention, the implants may be provided with a reservoir (e.g., drug layers) to incorporate one or more drugs into the implant to assist patients suffering from a variety of causes, including an infection of a prosthetic knee, hip, ankle or shoulder joint. Such reservoirs may be incorporated into any of the implants and devices discussed above. The terms reservoir or layer or drug layer are used interchangeably and meant to convey the nature of the function of the material containing an active agent or drug. A drug can be incorporated into and/or upon the implant using any suitable means, e.g., drug containing layers can be formed by preferential swelling in selected organic solvents and exposure to drugs dissolved in selected organic or aqueous solvents. The delivery of drugs through the controlled release from an implanted device provides a convenient and minimally invasive way of administering drugs over a sustained period.

Some embodiments of the invention are directed to a drug delivery system using a polymeric layer to form a drug reservoir into which a quantity of a drug may be stored in polymers which are comprised of phase separated polyurethanes. The invention may be used to deliver a wide variety of drugs. Some embodiments of the invention include a high capacity, polyurethane drug reservoir for controlled rate release administration of a drug formulation contained therein and a method for making such a drug delivery system. Other embodiments of the invention provide for the formation of layers within a polymer (e.g. a polyurethane) through processing and compositional changes which enable or improve drug loading capabilities. Such layers or reservoirs are able to deliver useful quantities of a drug, at relatively high rates if so desired. They may also reduce or in some cases eliminate the need for permeation enhancers.

In some embodiments, the polymeric drug delivery systems generally comprise a laminated composite of at least one layer that is substantially impermeable to the drug by virtue of not being swelled or loaded with drug and which provides an inner boundary of the system during drug delivery, and a high capacity reservoir in the form of a void or mixture of polymer and drug which was premixed prior to forming the drug delivery implant.

The drug formulation may be incorporated into the implant comprised from any of the polymers discussed above during formation of the implant or subsequent thereto. In some embodiments, the present invention describes a method in which a precast implant already generally in the form to be used in the body is exposed to a solvent in whole or in part to enable it to imbibe a specific drug. In such a procedure, a relatively greater degree of drug may be incorporated into the implant; that is, by absorbing drug after the implant has been prepared, drug loading of at least about 40 wt. %, and preferably on the order of 65 wt. % to 70 wt. % or higher can be achieved. It will be appreciated by those skilled in the art, however, that the various components of the reservoir may need to be varied to accommodate specific drugs.

The reservoir or layer will generally, although not necessarily, range in thickness from about 0.1 mm to about 10 mm. It will be appreciated that the thickness of the reservoir will depend, however, on a variety of considerations, including the quantity of drug to be incorporated in the reservoir, the rate of release, etc. It will be appreciated by those skilled in the art that any number of bulk configurations may be used in conjunction with the present drug reservoirs. Particularly bulk designs which serve other functions as replacement of sections of bone or cartilage or as scaffolding for tissue ingrowth or blood vessels.

The reservoir or layer may be formed from components in the polymer which may be described as macro, that is on a level of features which could be measured in terms of microns to millimeter or on a level which could be measured in terms of nanometers to microns. Micro features may depend more on the molecular structure and chemical composition of the polymer and local nanometer phase structure. Macro formations may be most conveniently described in terms of phase structure visible by light microscopy. Different phase structure and layers may be selected based on the drug being incorporated into the layer and its molecular size and chemical composition.

Secondary reservoirs may be constructed by preferentially swelling the polymer in two or more organic aqueous or combination of solvents which will permit the permeation of specific drugs into specific layers of the device. Secondary or primary layers may be conversely closed off from accepting a drug by exposure to inferior solvents. The layer is effectively deswelled or unswelled by, for example,

the removal of strong solvents as N,N-dimethylacetamide (DMAC) or tetrahydrofuran (THF) by the exposure to methanol or to solvents which are not good solvents for the drug being loaded into the reservoir.

The rate of drug delivery may be controlled in certain embodiments of the present invention. Within the scope of this invention, delivery includes delivery by cutaneous , transcutaneous, transdermal, transmucosal administration, i.e., delivery by passage of a drug through a layer or layers of polymer into body tissue or into body fluids or into or onto tissue adjacent to bone and into the bloodstream. In some embodiments, the reservoir is provided by means of differential swelling of specific layers within the polymer bulk by a first solvent. The rate controlling membrane or layer can be an unswelled or layer swelled in a second solvent. One or more additional reservoirs and/or adhesive layers may also be included by preferentially swelling the polyurethane in a second or third solvent. Rates may also be controlled by the addition of rate controlling molecules such as surfactants or chelating agents or nanocells which are not themselves pharmaceutically active but which serve to impede or augment the rate in which a drug permeates through the polymer layers. The system is preferably constructed such that an effective dose of a pharmaceutically acceptable agent will be delivered for a period in the range of days depending on the bulk of the polymer and depth of the layers.

Any number of drugs may be delivered using the reservoirs and drug delivery systems of the invention, i.e., any compound suitable for or transmucosal administration which induces a desired systemic effect. Such substances include the broad classes of compounds normally delivered through body surfaces and membranes, including skin. In general, this includes: anti-infectives such as antibiotics and antiviral agents, analgesics and analgesic combinations, anorexics, antiarthritics, antiasthmatic agents, anticonvulsants, antidepressants, antidiabetic agents, antidiarrheals, antihistamines, antiinflammatory agents, antimigraine preparations, antinauseants, antineoplastics, antiparkinsonism drugs, antipruritics, antipsychotics, antipyretics, antispasmodics, anticholinergics, sympathomimetics, xanthine derivatives, cardiovascular preparations including calcium channel blockers and beta-blockers such as pindolol and antiarrhythmic, antihypertensives, diuretics, vasodilators including general coronary, peripheral and cerebral, central nervous

system stimulants, cough and cold preparations including decongestants, hormones such as estradiol and other steroids including corticosteroids, hypnotics, immunosuppressives, muscle relaxants, parasympatholytics, psychostimulants, sedatives, and tranquilizers. The amount of active agent incorporated into the drug reservoir will vary, depending on the agent, the intended dosage, the individual undergoing treatment, the particular indication, and the like. The drug formulations contained in the reservoirs may also include standard carriers or vehicles useful for facilitating drug delivery, e.g., stabilizers, antioxidants, anti-irritants and crystallization inhibitors.

Steroids represent one class of drugs with which the present reservoirs and systems are particularly useful. Examples of steroid drugs which may be administered in conjunction with the invention include: progestogens such as flurogestone acetate, hydroxyprogesterone, hydroxyprogesterone acetate, hydroxyprogesterone caproate, medroxyprogesterone acetate, norethindrone, norethindrone acetate, norethisterone, norethynodrel, desogestrel, 3-keto desogestrel, gestadene and levonorgestrel; estrogens such as estradiol and its esters (e.g., estradiol benzoate, valerate, cypionate, decanoate and acetate), ethynyl estradiol, estriol, estrone and mestranol; and corticosteroids such as betamethasone, betamethasone acetate, cortisone, hydrocortisone, hydrocortisone acetate, corticosterone, fluocinolone acetonide, prednisolone, prednisone and triamcinolone.

Antibiotics represent another class of drugs that may be particularly useful with the present invention. The majority of hospital acquired infections of the joints are caused by the methycillin resistant Staphyloccocci, though other organisms and sometimes multiple organisms may be involved. Patients that have an infected prosthesis may experience pain, swelling, joint heat and osteolysis. If it is determined that the patient's joint is infected, the current procedure for addressing the infection includes removal of the infected prosthesis with cultures of tissue removed, sterilization of the joint via a Gentamicin loaded bone cement usually in conjunction with systemic antibiotics, immobilization of the limb, and re-implantation of a revision prosthesis after the joint is considered sterile. This procedure requires that the patient avoid weight bearing and mobility of the joint for up to six months while the joint is sterilized. The negative consequences seen with this current treatment

include; inflammatory reactions in the joint leading to scar tissue and contractures, muscle atrophy and bone loss.

An implant containing an antibiotic in accordance with the present invention may allow the patient to retain weight bearing activity and mobility of the joint during the sterilization phase leading to faster rehabilitation, better mobility and a more timely return to work for the patient.

Suitable compositions for use in the present invention are those polymeric materials that provide an optimal combination of properties relating to their manufacture, application, and *in vivo* use. In the uncured state, such properties include component miscibility or compatibility, processability, and the ability to be adequately sterilized or aseptically processed and stored. While the composition is curing, suitable materials exhibit an optimal combination of cure kinetics and exotherm. In the cured state, suitable compositions exhibit an optimal combination of such properties as abrasion, hardness, specific gravity, tear resistance, tensile strength, ultimate elongation, and biocompatibility.

The composition of the present invention provides a polyurethane that can be prepared *ex vivo*. Particularly when formed *ex vivo*, products incorporating the composition of this invention may be made in advance of their use, on a commercial scale, and under stringent conditions.

Polymeric biomaterials of this invention, including preferred polyurethanes can be prepared using automated manufacturing processes within the skill of those in the art. A preferred manufacturing method, for instance, includes the use of multichannel dispensing equipment to inject the polymer. Such equipment is well suited to high precision applications, having a variable or fixed number of channels, some have all channels dispensing the same volume while in others the volume can be set by channel, some have all channels dispensing the same fluid, while others allow for different fluids in different channels. The dispensing can be automated repetitive or manual. Suitable devices for metering, mixing and dispensing materials such as urethanes are commercially available from a variety of sources, including for instance from Adhesive Systems Technology Corp., 9000 Science Center Drive, New Hope, MN 55428.

Furthermore, polymeric biomaterials of this invention may be cured in a heated mold. The mold may receive the contents of the polymeric biomaterial before it is cured. In one embodiment, a permanent enclosed mold is used to form at least a part of the implant. Such a mold may be similar to a standard injection mold and have the ability to withstand large clamping forces. Further, such a mold may include runners and/or vents to allow material to enter and air to exit. Such a mold may be constructed from metals, polymers, ceramics, and/or other suitable materials. The mold may be capable of applying and controlling heat to the biomaterial to accelerate curing time. In some embodiments, the mold may be coated with a release coating agent to facilitate ease of removal of the cured biomaterial from the mold. Examples of suitable release agents include Teflon,™ silicone, florinated ethylene propylene (FEP), dichronite, gold, and nickel-Teflon combinations, various types of which are commercially available from a variety of sources, e.g., McLube Division of McGee Industries. In addition, the mold may be provided in two separable parts to further facilitate removal of the cured biomaterial.

Further, time and temperature parameters can be modified in processing to change the characteristics of the implant. A time temperature profile may be selected to achieve certain implant properties. In embodiments formed with a heated mold as described above, those skilled in the art will appreciate the manner in which both the temperature of the mold as well as the time biomaterial is maintained can be adjusted to change the characteristics of the molded implant.

In the embodiment in which an *ex vivo* curing polymer is used, the present invention preferably provides a biomaterial in the form of a curable polyurethane composition comprising a plurality of parts capable of being at least partially mixed at a time before use, the parts including: (1) a polymer component comprising the reaction product of one or more polyols, and one or more diisocyanates, and (2) a curative component comprising one or more chain extenders, one or more catalysts, and optionally, one or more polyols and/or other optional ingredients.

In some embodiments, long term congruence of the biomaterial is facilitated by its hydration *in vivo,* permitting the biomaterial to become more pliable, and in turn, facilitate congruence with the tibial plateau. In turn, an increase in hydration and/or changes in temperature can improve the fit and mechanical lock between the

implant and the tibial plateau. The biomaterial may be hydrated *ex vivo* and/or *in vivo*, both before and after the composition is cured. Preferably, the biomaterial may be further hydrated within the joint site after the composition in order to enhance both conformance and performance of the implant.

Implantable compositions of this invention demonstrate an optimal combination of properties, particularly in terms of their physical/mechanical properties, and biocompatibility. Such performance can be evaluated using procedures commonly accepted for the evaluation of natural tissue, as well as the evaluation of materials and polymers in general. In particular, a preferred composition, in its cured form, exhibits physical and mechanical properties that approximate or exceed those of the natural tissue it is intended to provide or replace. Fully cured polymeric (e.g., polyurethane) biomaterials within the scope of this invention provide an optimal combination of such properties as abrasion, compressive hardness, compressive modulus hardness, specific gravity, tear resistance, tensile strength, ultimate elongation, tensile modulus, and biocompatibility.

Polymers in accordance with the present invention may also be used as a tissue bulking agent. There are many situations where a tissue bulking agent is needed to address a clinical problem. Examples include female incontinence, ureterovisical reflex, post prostatectomy incontinence, gastroesophageal reflux, laryngeal plasty, foot pad bulking in diabetics, BKA stump padding (especially in diabetics), fecal incontinence and multiple applications in plastic surgery.

Some embodiments of the present invention include a bulking agent that comprises an injectable, biocompatible suspensions of inert particles that create a local non-inflammatory fibrotic reaction. Preferably, the particles are of a size (above 10 microns,) that doesn't allow them to be engulfed by phagacytic cells, thus preventing migration. Further, they can have a specific gravity of around one so that they may stay in suspension in a viscous physiologic carrier like hyaluronic acid and they may be free of any toxic leachable material that might be released in a physiologic environment. Any of the polymers discussed above may be utilized in such a tissue bulking agent. In some embodiments, the biopolymer is cured, and then particulatized by any suitable method (e.g., ball milling).

The tissue bulking agent of the present invention may comprise a variety of useful forms. In some embodiments, the tissue bulking agent comprising an injectable biocompatible suspension of polyurethane particles. Such embodiments may contain particles between 10 microns and 100 microns, in their largest dimension. Further, the tissue bulking agent may be contained in a suspension media comprising a biocompatible fluid or gel, such as a solution of hyaluronic acid.

PHYSICAL/MECHANICAL PROPERTIES AND TEST METHODS

Various properties of the composition of this invention can be evaluated for use in quality control, for predicting service performance, to generate design data, to determine compliance with established standards, and on occasion, to investigate failures. See, for instance, Handbook of Polymer Testing: Physical Methods, edited by Roger Brown, Marcel Dekker, Inc., New York, New York (1999), the disclosure of which is incorporated herein by reference. Suitable properties include those dealing with a) mass, density and dimensions, b) processability, c) strength and stiffness (including compressive hardness, compressive modulus, tensile stress-strain, flexural stress-strain, flexibility, and tear tests), c) fatigue and wear (including abrasion resistance and hardness), d) time dependent properties (such as creep, stress relaxation, compression set, tension set), e) effect of temperature (such as thermal expansion, shrinkage, and thermal oxidative aging), f) environmental resistance, and g) and biocompatibility parameters.

Of particular note are those properties that lend themselves to the preparation, delivery and long term use of improved implants having an articulating surface, and preferably for long term weight bearing use..

The preferred property ranges given below are only relevant to certain embodiments of the invention. It will be appreciated by those reasonably skilled in the art that materials having one or more properties outside the scope of the preferred ranges given below are suitable for use with the present invention.

Abrasion values for a polymer can be determined with a rotating cylindrical drum device, known as a DIN abrader. A loaded cylindrical test piece is traversed along an abrasive cloth attached to a rotating drum, and the mass loss is measured after a specified length of travel. Advantages of this device include the use of a test

piece small enough to be cut from a product or a comparatively thin sheet and a much reduced risk of abrasive contamination caused by debris or smearing. The result can be expressed with the abrasion resistance index, which is the ratio of the volume loss of a black standard rubber sample to the volume loss of the test sample.

The polymer preferably provides a DIN abrasion value of less than about 70 mm^3, more preferably less than about 60 mm^3 and most preferably less than about 50 mm^3, as determined by ASTM Test Method D5963-96 ("Standard Test Method for Rubber Property Abrasion Resistance Rotary Drum Abrader"). DIN abrasion values of greater than about 70 mm^3 tend to exhibit wear rates that are too great for longer term use as articulating surface.

Abrasion may also be assessed in terms of wear resistance. Wear resistance may be determined with a knee simulator or an Instron Stanmore simulator. As an example, a knee simulator may be a servo-position controlled mechanical test system designed to simulate the primary forces and motions which a knee implant may encounter during its clinical use in a temperature controlled fluid environment. The simulator may provide simulation of femur flexation, pneumatic vertical force application, cyclic vertical displacement, cyclic horizontal displacement of a simulated proximal tibia which holds a polymer implant, and passive rotation of the tibial implant holder. Axial force, flexation, AP (horizontal), roll and slide, and axial rotation may be provided by stepper motors. An electronically controlled pneumatic system may use axial force provided feedback to a pneumatic servo controller to maintain an appropriate force level. For further description of a knee simulator and Instron Stanmore simulator, see Paul J. Buscemi et al., Mechanical Test System for Knee Prosthesis, Society for Biomaterials 28th Annual Meeting Transactions, 307 (2002).

Biomaterial can be formed into standardized (e.g., puck-like) implant shapes and subjected to conditions intended to replicate, while also meet and exceed physiological conditions. Preferred biomaterials of this invention are able to withstand one million cycles (approximately equivalent to 1 year implantation), and more preferably greater than 5 million cycles (approximately equivalent to 5 years) on a knee simulator as described above before generating unsuitable debris.

Flexural stress/strain fatigue can be measured in a variety of ways. Using the standardized shape as described above, samples can be compressively loaded in cycles of increasing loads, and the stress strain fatigue can be plotted verses the number of cycles.

As another example, flexural stress/strain fatigue can be determined by a three point bending test, in which a standardized implant sample shape is supported at its anterior and posterior ends. A cyclical load is applied to the sample in an area substantially between the two supports to provide a deflection of approximately 4 mm, and the total number of cycles until failure is recorded.

Biomaterials formed into implant shapes in accordance with the present invention, under conditions intended to meet and exceed physiological conditions, are preferably able to withstand one million cycles (approximately equivalent to 1 year implantation), and more preferably greater than five million cycles (approximately equivalent to 5 years implantation) in a test similar to the one described above.

Fracture toughness can generally be determined by a number of methods. For example, fracture toughness can be measured by tests similar to ASTM Test Method D5045-99.

Preferably, the polymer provides a peak load fracture toughness of at least about 50 lbs, more preferably more than about 80 lbs, and most preferably more than about 110 lbs. Further, the polymer preferably provides an energy to break fracture toughness of greater than about 15 lb-in, more preferably greater than about 25 lb-in, and most preferably greater than about 30 lb-in. These values may be obtained with tests similar to ASTM Test Method D5045-99.

The term hardness has been applied to scratch resistance and to rebound resilience, but for polymers it is taken to refer to a measure of resistance to indentation. The mode of deformation under an indentor is a mixture of tension, shear, and compression. The indenting force is usually applied in one of the following ways: Application of a constant force, the resultant indentation being measured, measurement of the force required to produce a constant indentation, or use of a spring resulting in variation of the indenting force with depth of indentation.

A biomaterial of this invention preferably provides a hardness value when hydrated of less than about 75 Shore D, more preferably less than about 70 Shore D,

and most preferably less than about 60 Shore D, as determined by ASTM Test Method D2240. In some embodiments, hydration of the biomaterial may lower the shore hardness value to less than about 60 Shore D to provide for greater congruency of the implant to the joint in situ.

In one method of determining specific gravity, a test piece is provided weighing a minimum of 2.5 grams, which can be of any shape as long as the surfaces are smooth and there are no crevices to trap air. The test piece is weighed in air and then in water using a balance accurate to 1 mg. The test piece can be suspended by means of a very fine filament, the weight of which can be included in the zero adjustment of the balance and its volume in water ignored. The specific gravity is calculated from the difference in measurements.

The polymer preferably provides a specific gravity of about 1 g/cm^3 to 2 g/cm^3, more preferably about 1 g/cm^3 to 1.5 g/cm^3, and most preferably about 1.15 g/cm^3 to 1.17 g/cm^3, as determined by ASTM Test Method D792.

A tear test may be used to measure tear strength. In a tear test, the force is not applied evenly but is concentrated on a deliberate flaw or sharp discontinuity in the sample and the force to produce continuously new surface is measured. This force to start or maintain tearing will depend in a complex manner on the geometry of the test piece and the nature of the discontinuity.

Preferably, a biomaterial of this invention provides a tear strength value in the Die C configuration of greater than about 400 pounds per linear inch (PLI), more preferably greater than about 600 PLI, and most preferably greater than about 800 PLI, and a value in the Die T configuration of preferably greater than about 100 PLI, more preferably greater than about 150 PLI, and most preferably greater than about 250 PLI, as determined by ASTM Test Method D624.

To measure tensile modulus, tensile strength, and ultimate elongation, a test piece of the material is stretched until it breaks, and the force and elongation at various stages is measured. A tensile machine is used to perform this test. Generally, the basic elements of a tensile machine are grips to hold the test piece, a means of applying a strain (or stress), a force-measuring instrument, and an extensometer.

The polymer preferably provides a tensile modulus at 100% elongation value of about 1,000 psi to 10,000 psi, more preferably about 2,000 psi to 5,000 psi, and most preferably about 2,500 psi to 4,500 psi , as determined by ASTM Test method D412.

The polymer preferably provides a tensile modulus at 200% elongation value of about 1,000 psi to 10,000 psi, more preferably about 2,000 psi to 6,000 psi, and most preferably about 2,500 psi to 5,000 psi, as determined by ASTM Test method D412.

The polymer preferably provides a tensile strength value of greater than about 6,000 psi, more preferably greater than about 6,500 psi, and most preferably greater than about 7,000 psi., as determined by ASTM Test Method D412.

Preferably, the polymer provides an ultimate elongation of greater than about 200%, more preferably greater than about 250%, and most preferably greater than about 275%, as determined by ASTM Test Method D412.

To measure compressive modulus and compressive strength, a sample is again formed in a standardized (e.g., puck) shape and varying compressive loads are applied to the sample in order to develop a corresponding curve. The compressive modulus can be determined from this curve. Compressive strength may be determined by applying increasing loads to a sample until the sample fails.

Preferably, the sample implant provides an compressive modulus of greater than about 4,000 psi, more preferably greater than about 4,500 psi, and most preferably greater than about 5,000 psi, as determined in the manner described above. In some embodiments, the compressive modulus may be greater than about 16,000 psi.

Preferably, the sample implant also provides a compressive strength of greater than about 6,000 psi, more preferably greater than about 7,000 psi, and most preferably greater than about 8,000psi, as determined by a test similar to the one described above.

Water absorption may be determined in a variety of ways. A suitable method for measuring water absorption is to submerge a sample of the test material, with an implant-type geometry, in a saline solution. Once the sample and saline solution

reach equilibrium at 37 degrees Celsius, which may take a month or longer, the sample is removed and weighed to determine its water absorption.

Preferably, the polymer provides a water absorption value less than about 5% at 37 C, more preferably less than about 3% at 37 C, and most preferably less than about 2% at 37 C, as determined by a test similar to the one described above. In some embodiments, implants inc accordance with the invention absorb fluids (e.g., water) in vivo, which may soften the material and add cushioning properties.

The medical-grade polyurethane resins were evaluated for biocompatibility in accordance with ISO 10993: Biological Evaluation of Medical Devices and FDA G95-1: Required Biocompatibility Training and Toxicology Profiles for Evaluation of Medical Devices. The biological effects of the resin, such as cytotoxicity, sensitization, genotoxicity, implantation, chronic toxicity, and carcinogenicity, were studied. The tests were conducted in accordance with the FDA Good Laboratory Practice (GLP) Regulation.

The following tests were conducted to determine if the polymer is biocompatible: 1) ISO MEM elution using L-929 mouse fibroblast cells; 2) ISO agarose overlay using L-929 mouse fibroblast cells; 3) ISO acute systemic injection test; 4) ISO intracutaneous reactivity test; 5) ISO guinea pig maximization sensitization test; 6) Material mediated rabbit pyrogen test; 7) In vitro genotoxicology test; and 8) ISO muscle implantation study in the rabbit with histology-1 week. The results of the eight selected screening biocompatibility tests above show that the polymer passes all the tests and is considered biocompatible.

The present invention also includes methods for predicting the wear of a polyurethane device bearing on osteoarthritic bone, including a tensile test and a composition correlation. Numerous researchers have attempted to develop methods which predict wear of orthopedic devices during physiologic conditions. A comprehensive review by Clark list some of the early studies. In Clark, IC Wear Screening and Joint Simulation studies vs. Materials Selection and Prosthetic Design, Clinical Reviews in Biomedical Engineering, 8 issue 1, 29-90, 1982, the contents of which are herein incorporated by reference, some of the early studies in this area are reviewed. Most studies are concerned with the wear of polyethylene against smooth metal surfaces used in the typical total knee or hip replacement devices. Relatively

few studies have aimed at the wear of materials against bone. The present invention includes a tensile test and a wear test which produce results that mimic a full scale knee simulation in which the implanted device is placed against osteoarthritic bone.

Previous researches have demonstrated aspects of various types of wear testing. One of the more general and applicable concepts is that of a critical point as describe in Cho K Lee D, Effect of Molecular Weight Between Cross-links on the abrasion behavior of rubber by a blade abrader, Polymer 41 (2000) 133-140 1999(2), the contents of which is hereby incorporated by reference. Wear is found to proceed primarily by fatigue below this point and above which wear is dependent on abrasion or perhaps a combination of abrasion and fatigue. In Cho's work, the critical point was found to be a function of the crosslink density and corresponded to the fracture energy of the polymer. In Thavamani P, Khastgir D, Bhowmick AK, Microscopic studies on the mechanisms of wear of NR, SBR and HNBR vulcanizates under different conditions, Journal of material Science, 28 6318-6322, 1993, Steijn RP, Friction and Wear in Friction and Wear of Polymers, Bartenev et al GM Amsterdam NY, 19, 357-381 , 1981, and Gent AN Pulford CTR, Mechanisms of Rubber Abrasion, J. Applied Polymer Science, 28, 943960, 1983, the contents each of which is hereby incorporated by reference, a critical point is described in terms of load and the appearance of Schallamach waves. In Persson BNJ, Tosatti E, Qualitative theory of rubber friction and wear, J chem. Physics vl 12, no 4, 2021-2029, 2000, the contents of which is herein incorporated by reference, a similar phenomenon is described in terms of whether or not a polymer responds in an elastic or plastic mode which is related to crosslinking and temperature.

Several other factors influence wear during practical testing, such as the effect of temperature.. In Grosch KA, The relation between the friction and visco eleastic properties of rubber, Proc. R. Soc. A 274 21-40 1963, Furukawa J, Chemical Aspects Concerning the Friction and Abrasion of Rubber, Bull Chem. Soc. Jpn, 69, 2999-3006, 1996, and Ahagon. A, Theory of rubber abrasion, International Polymer Science and Technology 23, n6 t/32-t/29 1996, the contents each of which is hereby incorporated by reference, small changes in temperature, on the order of 5 degrees, were demonstrated to significantly alter wear rates in disproportion to the temperature rise. In Ahlroos T, Saikko V, Wear of prosthetic joint material in various lubricants,

Wear, 211, 113119, 1997, and Saiko v, A multidirectional motion pin-on-disk wear test method for prosthetic joint materials, J Biomed Mater Res, 41, 58-64, 1998, the contents each of which are hereby incorporated by reference, the effects of the type of lubrication, whether or not the wear directions is one or two dimensional, and if motion is cyclic or not as important considerations have been discussed.

The knee wear simulator used in conjunction with this work is denoted as the Knee Motion Machine (KMM) to distinguish it from knee simulators which use muscle simulation. For a discussion of the KMM, see Buscemi PJ, Alberts R, Haider, H., "Mechanical Test System for a Knee Prosthesis", 28th Annual Meeting, Society for Biomaterials, Tampa, Florida, 2002., the contents of which is hereby incorporated by reference. The KMM has been used to simulate actual physiological conditions in the knee and to identify products of wear. It is a position controlled machine. Motions for flexion, anterior /posterior displacement and load profile are described by in Chassin EP, Kikosz RP Andriacchi TP, Rosenberg AG, J Arthroplasty vl 1, no5 553-559, 1996, the contents of which are herein incorporated by reference, for unicompartmental loading with a maximum load of 1600 N. Wear results of devices tested on the KMM compare favorably with explanted devices in terms of retrieved particle size and particulates on implant surfaces, surface morphology, wear areas and location, and the presence and spacing of Schallamach waves. However, KMM testing is relatively expensive and time consuming.

The following discussion generally describes the equipment and methods used for performing the wear testing. Of course, other equipment and/or methods may be used to perform such testing. The mechanisms of wear are sufficiently complex in general and particularly so in a bone on polymer system that incorporating approximate in-use conditions into the test protocol may narrow the range of sources of discrepancies making it easier to obtain useful predictive information from shorter duration testing. For instance, in contrast to most wear testing for orthopedic devices, testing in this instance requires a relatively rough surface. The surface of arthritic bone is composed of not only area of partial coverage cartilage but also of eburnated or bare roughened bone which is perforated with pores 20 to 200 micrometers in diameter as shown in Figure 22.

The wear method used for KMM screening is largely based on certain aspects of KMM testing: a reciprocating motion, relative velocities of 6 to 8 cm/sec (the femoral condyle transverses 3 to 4 cm in 500 msec. over the top of the polymer), a lubricated system, limited third body wear, loads between 2 to 5 MPa, controlled temperature, and, as mentioned above, a relatively rough surface compared to most orthopedic wear testing (70 microns vs .1 to 2 microns). In some embodiments a Buehler Ecomet polisher (sometimes referred to herein as the Buehler or the Buehler method). The Buehler may use a 12 inch diameter lower CCW and a rotating 12 in diameter platen with an abrasive surface and an opposing CCW rotating 7 inch diameter sample holder. The platen may be covered with a diamond impregnated plate (Buehler 15-6270) with a nominal particle size of 70 micrometers. Other coarseness levels may be used. In actuality, the surface may be composed of islands 1 mm diameter of the diamond particles spaced approximately 0.2 mm apart as shown in Figure 23, on a polisher as shown in Figure 24. The space between islands of abrasive decrease particulate loading on the bearing surface during the test and mimics the smoother areas of bone. The sample holder is allowed to pivot freely to equally load the three specimens. The sample holder is loaded to 66N normal to the platen and is placed tangent to the platen within 2 to 3 mm of the edge. It was found during test development that in using silicon carbide rather than a diamond plate wear rates decrease during the test and it is not recommended.

In some embodiments, water from a 20 L container is circulated by a submersible pump at a rate of 500 ml/min onto the surface of the platen and back to the container through a 2 micron fibrous filter. The duration of the test is preferably one hour. During this time no noticeable change may occur in the cloudiness of the water but the filter may become loaded with particles. Temperature may be controlled 30 C ± 1 C using an auto tuning solid state controller (Watlow 935A) and a submersible heater (Visi-Therm model VTN 100). The mass and large surface area of the platen, large water volume and flow help maintain a constant temperature.

For each Buehler test, three specimens, between 7 mm and 12 mm thick, were cut from sheets or molded parts to a diameter of 16 mm using an ASTM D 5963 abrasion specimen cutter. For assessment and quantification of wear, each specimen may be separately weighed before and after each test and the total weight averaged at

the end of the run. Individual specimen weighing gives an indication if adverse conditions arose during the test procedure as does the live time recording from the position sensor.

The specimens may be held in place in the sample holder using three custom fabricated polyurethane adapters. Each adapter may have a depression 3 mm deep and 16 mm diameter, and be fitted with a circular disk of 240 grit adhesive backed SC paper (Buehler part 30-5112-320-psa) which prevents the specimen from spinning in the depression. The specimens may be pressed into the polyurethane specimen holders with modest pressure. The Beuhler polisher may be programmed to run at 80 rpm CCW for the platen, 60 rpm CCW for the sample holder, 15 lbs and 60 min. producing a nominal stress of 0.1 MPa. The vertical position of the sample holder may be monitored using a linear position sensor with a sensitivity of > .01 mm. (Omega part #234234) operated at 5v from the computer. Data collection may be through a WinDaq A/D converter and XL plug-in (DataQ Instruments, Springsdale, OIL for Excel software (Microsoft).

The following discussion generally describes the equipment and methods used for performing the tensile testing. Of course, other equipment and/or methods may be used to perform such testing. For tensile testing, specimens were cut from sliced cross sections of finished device or from sheet stock to 2 to 3 mm width using a dogbone die with a 2 mm center width and length of 25 mm. The prepared specimens were pulled at a crosshead speed of 25 cm /min with a MTS Bionix 400 was tensile machine. A minimum of six specimens were pulled for each material and data was automatically recorded.

NCSS (NCSS, Inc Kaysville, Utah) statistical software was used for regression analysis of the tensile data. Prism statistical graphing software (GraphPad, Inc) was used for linear regression presentation. The regression analysis included the following components: Ultimate tensile strength (UTS), % elongation, Young's modulus , modulus at yield, strain at yield. Of these parameters, % elongation, % strain at yield, and modulus at yield were found to correlate with wear. UTS, stress at failure, peak stress, Youngs's modulus did not enter the calculations. Standard deviation for tensile results were generally less than 7 % and rarely over 10 %.

Wear was estimated using: a) % elongation recorded as a fraction, b) % strain at yield, and c) modulus at yield. Equation 1 was developed from a multiple regression with forward hierarchical switching of order three and a maximum of three terms.

$$W = 364/e + 13986/y - 85381/(y * s) \qquad \textit{equation 1}$$

Where

y = modulus at yield in MPa,

e = elongation as a decimal, and

s = % strain at yield.

Several types of materials were tested and used for comparative analysis. Gamma crosslinked ultra-high molecular weight polyethylene (UHMWPE) supplied by DePuy, Thermedics (Wilmington MA) Carbothane 72 D and 55D and Dow Pellethane 2363 80AE and 72 D were supplied by the manufacturers. Materials designated as PU80A, PU72D and PU 55D were commercially available carbon black filled polyurethanes. A PVC material (Wimdos Corp., St Could MN formulation 1012G) was also used. The materials used to generate the regression coefficients are listed in Table 1.

A series of polyurethanes formulated in-house were also analyzed and are listed in Table 1 as PUF1-PUF8. These polyurethanes contain amethylenediphenyldiisocyante (MDI), polytetramethylene oxide (PTMO), and 1,4 hydroxyterminated butyleneoxide (BDO) based polyurethanes with a composition similar to that of Pellethane 55D except that 3% trimethylolpropane (TMP) was added as a crosslinking reagent. These were injection cast as a two part system into heated metal molds. These materials contained 58 wt% hard segment and have elongations near 350%. The difference between PUF1 and PUF8 materials is the temperature of the casting process. Molding temperature caused measurable changes in the mechanical and wear properties. PUF4 and PUF6 were also manufactured in-house. These are softer materials than the PUF1 and PUF8 polyurethanes. PUN and PUF6 contain 45 wt% and 22 wt% percent hard segment and have elongations of 280% and 600% respectively. All in-house produced materials were annealed for a minimum of

24 hours at 120° C and used after at least six days post manufacture. Manufacture and testing was performed over a four month period.

Table 1 lists the materials wear tested and used in the regression analysis along with the estimated results from the tensile testing. Table 2 list those wear tested and whose wear was estimated solely using equation 1. A linear regression of the predicted wear vs actual wear is shown in Figure 25. The correlation between the actual versus the estimated wear is often less than 10%.

Materials Used to create Regressive model						
	Actual wear Ave ±10%SD mg	Estimated wear from Regression mg	% Difference	Tensile elongation @ break/100 fraction	% Strain @ Yield	Modulus @ yield MPa
UHMWPE xlinked GVF	60-65	62.87	0.2	1.3	1.4	216
Pellethane 80A	210	238.36	13.5	5.8	24.9	54
Carbothane 72d	156	189.48	21.5	1.49	2	81.5
Carbothane 55d	197	196.36	0.3	1.83	8.3	216
Pellethane 55d	189	168.75	10.7	2.58	12.6	152
PUF4	410	420.06	2.5	2.83	22.6	32.8
PVC	1000	959.50	4.1	1.85	50.2	15.7

Table 1 Materials and tensile parameters and result. The wear values are for 20 min of testing corresponding to a KMM test of 300, 000 cycles. These materials were used to generate the regression coefficients. Values for estimated wear are from equation I.Statistical data for the multiple regression: hierarchical with switching 3rd order,R2=.9877, Coef variation = .1610, mean sq error= 1759

Estimated Wear for Materials via Equation 1. These materials were not used in determination of the regression coefficients						
	Actual wear for 20 min of Buehler testing mg	Estimated wear mg	% Difference	Tensile elongation @ Break/100	%Strain @ Yield	Modulus @ yield MPa
PUF1	130	149.30	14.8	2.9	8.6	136
PUF6 lot 1	110/ 600*	746.81	24.5	4.97	34.5	16.6
PUF6 lot 2	122 / 700*	621.48	11.2	6	36	20
PUF9-5 lot 1	145	163.01	12.4	3.6	15.8	105
PUF8-5 lot 1.	159	147.56	7.2	3.6	14	119
PUF8-5 lot 2	152	149.98	1.3	3.97	14.3	102.58
PUF8-5 lot 3	100	113.15	13.2	3.46	9	162
PUF8-lot 1	181	158.57	12.4	3.05	12	116.4
PUF8-lot 2	153	176.68	15.5	4.29	18.5	83.9
PUF8-lot 3	135	126.37	6.4	3.35	10.8	162
PUF8-lot 4	100	113.15	13.2	3.46	9	162
PU 80A	429	411.66	4.0	6.72	12.5	18.96
PU 90A	178	200.79	12.8	2.7	11._7	78
PU 75D	420	385.49	8.2	0.9	6.2	564.7

*Table 2: Materials and parameters used to estimate wear and Buehler results. The materials listed as PUF1-8 are MDI, PTMO, BDO based polyurethanes with a composition similar to that of Pellethane 55D except that 5% TMP was added as a crosslinking reagent. Differences in the materials were due to the temperature of the casting process. PUF6 was a softer polyurethane and * indicates a discrepancy in wear values which is explained in the text. The last three materials were commercially available polyurethanes. Equation 1 was used to estimate wear from the tensile data.*

During test development, specimens were removed periodically to reweigh to determine mass loss over a one hour period. Because realignment of the specimens was difficult and time consuming, a position sensor was added to provide a method to continuously examine wear progress. Wear rate was then determined from a plot of the total weight loss of the specimen to the total motion of the sensor. The rate of mass loss was determined from the slope between five and 50 minutes of the sixty minute test. The test conditions were adjusted so that mass loss from UHMWPE was 64 mg. Deviation from linearity in this time frame was less than 0.2%. For comparison to KMM data, the rate of mass loss from Buehler testing was multiplied by 20 min. corresponding to the mass loss of this material during 300,000 cycles of KMM testing.

To investigate the effect of speed and roughness of the abrasive surface, several tests were conducted with three materials under slightly different conditions. UHMWPE, Pellethane 80A , and PUFI were run using 400 and 600 grit paper and, 20 lbs load, 20 min test run time and 40, 80 and 120 rpm for the platen as shown in Figure 26 (which shows wear rate as function of rotational speed of the platen at 600 grit SC paper, and PE120 = UHMWPE @120 rpm, Pel 80= Pellethane 80A@ 80rpm, etc) and Figure 27 (which shows the same materials as Figure 26 tested as a function of surface roughness using 400grit and 600 grit silicon carbide paper). The following parameters were used for both tests: 20 min, 20 lbs, 80 rpm platen speed, and n>12. While the increased speed did show, as expected, an increase in wear for a 20 minute run time, the rate did not increase when normalized to distance (total revolutions). In fact, for the polyurethanes and UHMWPE, normalized wear decreased for 80 rpm and then increased slightly for 120 rpm. (Table 3).

Material – rpm	Pel-40	PUF1-40	UHMWPE-40	Pel-80	PUF1-80	UHMWPE-80	Pel-120	PUF1-120	UHMWPE-120
mg loss RPM Normalized	80	96	54	75	75	33	106	106	40

Table 3. Mass loss normalized to 40 rpm for three materials under. For PUFI there is a 7% decrease in mass loss at 80 rpm and a 20% increase when the rotational speed is tripled. Normalized UHMWPE mass loss also decreases for both higher speeds.

Several materials were tested using KMM Buehler and tensile methods. Some of the results are shown in Table 4 normalized for 20 minutes of Buehler testing (300,000 cycles of KMM testing). Buehler conditions were adjusted to match the KMM wear and it was also used in the regression analysis. UHMWPE was therefore used essentially as a control for all three methods. PUF4 was used in generating the regression coefficients so it would be expected to correlate in the comparison of Beuhler testing vs. tensile data, but the KMM wear value for PUF4 also correlates well. The various types of PUF1 were not used to generate equation 1.

Material	KMM Testing mg	Buehler testing 20 min mg	Tensile Results mg
UHMWPE	64	64	62
PUF4	400	410	420
PUF8	134	108	154
PUF1	120	130	135

Table 4. Comparison of KMM, Buehler and tensile results for three materials. Results for PUFl have a range because of slightly different conditions of preparation and casting. PUF4 has a lower hard segment content. Each of the values represents averages from at least 10 specimens with for the KMM 20%, and under 10% for tensile and Buehler testing

From Table 4, modulus and strain at yield appear to be significant indicators of wear. This is exemplified in Figures 28 and 29 in which wear on the vertical axis is plotted against 1/elongation and either 1/modulus at yield (Figure 28) or 1/yield strain (Figure 29). While wear is shown to be generally inversely proportional to modulus and elongation, unexpectedly, the surfaces of the plots are continuous but not smooth having peaks and valleys. This was initially thought to be due to gaps in the data from the materials selected for testing.

To investigate the non- uniform curvature, a plot of 600 hypothetical sets of elongation, strain and modulus between 100 to 400%, 5 to 10 %, and 100 to 200 MPa was constructed and is shown in Figure 30. The plot did not become smoother, it became more convoluted. This plot shows a discreet valley as a function of 1/ yield modulus near for all lower elongations. In the valley, wear decreases for lower elongation. The model appears to indicate that at low elongation, there are combinations of yield strain and modulus that produce low wear. At high elongation, the higher the modulus, the higher the resistance to wear. At higher elongations, the effect of modulus is more continuous and modulus and elongation contribute to good wear.

When different data sets are used, either incorporating more materials, or a different range of materials, different equations may be generated. The same three parameters may be selected but the number of terms and order may be different. Equation 1 has been found to be a simple form of yielding results with low standard deviation and acceptable consistency. It may be more important to note that the UTS, modulus and strain at yield are selected as material properties to use in the equation rather than the specific regression equation which uses them.

Third body wear does not likely play a major role in the wear process in the Buehler testing. Particles are trapped in between the island of diamond abrasive, but few are seen on the surface of the islands after a test. The large volume of lubricating water also reduces this risk. Additionally, even after repeated runs of several hours with the same lubricant, the wear of UHMWPE remains constant as long as the platen is cleaned after each run.

Wear was not found to be proportional to velocity for three materials when normalized to distance (revolutions) and in fact, were found to decrease slightly. The reasons for decrease are not understood at present. Melting of the polymer probably did not occur because of the lubrication. It may be more a function of the relative position or direction of the sample holder on the platen rather a velocity issue or how well water was dragged between the specimen and platen. Wear was found to be strongly correlated to roughness of the surface as the abrasive surface was increased from 600 to 400 grit (15 to 22 micron), the material loss increased from 150 to 240 mg. However, increasing the frequency of the KMM flexion cycle from 1.2 hz to .8 can have enormous effects. The difference lies in the temperature difference that the KMM can generate on the surface of the polymer at high loads particularly after heel strike. As an indirect indication, we have seen that bovine serum, which is often used for lubrication, is for all practical purposes cooked during knee wear simulations. Thermocouples placed within test specimens also show increase in temperature. An increase in temperature of 10 deg C in the Buehler testing, by heating the lubricating solution, can result in increased wear rates.

The regression coefficients are based on the wear obtained from the Buehler measurements using specific speeds and loading. If such conditions as lubricant type and particularly temperature are altered the coefficients would be expected to change. The conditions used here are suitable when materials are subjected to wear testing that places the material in an abrasive regime. If the material is placed under milder conditions, the predicted wear will be much higher than that produced by the Buehler testing using this set of coefficients. This occurred for the material denoted as PUF6, a softer material with an elongation of over 600%. However, if PUF6 is subjected to forces which bring it into the frictional range - doubling the force for example rather than the wear rate increase in proportion to the applied pressure as Pellethane 55D does, the wear increases by a factor greater than 5 placing the Buehler wear results close in line with the results predicted by the tensile testing. It is not known that if the tensile parameters were based on fatigue rather than abrasion if the results would have been as good.

Fracture toughness was investigated as a potential predictor but to a much lesser extent. However, it does appear that some fracture parameters can be used to produce an even better correlation to wear. Specifically, the stress at yield for materials is significant as a predictor and is largely independent of the slit width used in the fracture test. It may be useful to combine fracture and tensile values at yield to provide indicators for wear. Conversely, fracture toughness (stress extrapolated to zero slit length) is highly dependent on geometry and we found as in Mardel JI, Hill AJ, Chynoweth KR, Wear resistance of polyurethane elastomers, Materials Forum, 16, 155-161, 1992, the contents of which are herein incorporated by reference, that fracture toughness does not provide useful predictive information.

Predictive estimation of wear with a precision of 10% is useful. It should be noted that slightly different processing conditions produced measurable changes in Buehler testing results tensile properties. These differences became apparent for all three methods of evaluation. It appears that wear can be estimated within this range using both the Buehler and tensile testing methods, but the conditions of testing must be specified. The particular parameters of loading, lubrication, abrasive roughness, and particularly specimen heating effect the ability of a polymer to initially withstand an assault -overcome by modulus and yield - and then to recover through sufficient elongation. It appears that a balance of modulus and elongation provide properties for reducing wear in a particular circumstance.

Composition of the polymer may also be used to predict wear as long as the composition variation is not too great. If done properly, regression analysis should be able to use independent variable of compositions to create `vectors' which point towards improved wear. Compositional data which also has associated wear data or tensile data has been used to develop an equation with independent variables of moles of composition to predict wear.

The regression is based on the dependent variable, wear, which is determined by Buehler testing for a 20 min run normalized to UHMWPE. Wear predicted by the tensile test and that by Buehler are essentially equivalent and both were used with equivalent results. The components are written as moles x 1000 in Table 5 to avoid

the use of values < 1. A multiple regression (forward with hierarchal switching) was run on statistical software with the following results.

Table 5		Moles x 1000					
Material	Wear mg	MD1	T 1000	T2000	TMP	BDO	Predicted Wear mg
A	621	80	29.3	23.98	0.6	23.78	626.7
B	2600	90.84	27.96	22.68	0.61	37.22	2602.
C	746	115.72	24.77	19.65	0.9	70.56	729.46
D	410	147.63	23	11.5	30	90.4	413.42
E	150	180.86	23.8	9.03	1.66	141.02	161.30
F	221	156		24	0.35	132.89	

The following are the statistical parameters used in this embodiment:

The following model equation generated from the regression:

Parameter	**Value**	**Parameter**	**Value**
Dependent Variable	wear	Rows Processed	6
Number Ind. Variables	4	Rows Filtered Out	0
Weight Variable	None	Rows with X's Missing	1
R2	0.9999	Rows with Weight Missing	0
Adj R2	0.9998	Rows with Y Missing	0
Coefficient of Variation	0.0234	Rows Used in Estimation	5
Mean Square Error	450.07	Sum of Weights	5.000
Square Root of MSE	21.21	Completion Status	Normal
Completion			
Ave Abs Pct Error	2.318		

Wear = (971.4415607*T2000) - (47.284007957*BDO *T2000) +
(1.8006199*BDO*T1000*T2000) –
(1.53068458*T1000*T2000*T2000) Eqn 2

where T1000, T2000, and BDO equals the composition of each respective component in moles.

Note that MDI does not appear in the equation but it is not an independent variable since the number of moles of MDI equals approximately five other components. Also there is nothing particular to this equation, regression analysis of slightly mole fractions could yield different regression coefficients. In addition, there is nothing in the equation that takes into account the morphology of the polymer. That is accounted for in the wear test. If morphology drastically alters the wear results, then this will be portrayed in the equation. Conversely, if the equation can not cope with drastic alterations, then the R values will be poor.

The equation was used in an Excel macro to generate the Table 6 showing sample wear values using mole compositions near a specific composition F100 noted above. e.g for 100 Wt% MDI in F100 => 0.18 moles so values from 0.17 to 0.19 x 1000 were used in the equation. Over 65000 combinations were evaluated, about 1000 selected, and 35 are presented. The selection range was 20 mg < wear < 190 mg. Note the nearly constant values for the ratios of BDO to MDI and T1000. The model predicts that widely varying values of MDI can be used to produce equivalent wear as long as the mole ratios of BDO/T1000 and MDI /BDO remain near 6 and 1.2 respectively. For reference, the wear for F100 - 150 mg and 65mg for HMWPE.

Table 6: Sample Values – Composition is in moles x 1000

Predicted Wear mg	MDI	T 1000	T 2000	TMP	BDO	BDO/T1000	BDO/T2000	MDI/BDO
20.43	190.00	23.75	7.00	1.25	158.00	6.65	22.57	1.20
21.03	180.00	24.80	16.00	1.20	138.00	5.56	8.63	1.30
21.06	165.00	22.80	3.00	1.20	138.00	6.05	46.00	1.20
22.36	185.00	23.55	6.00	1.45	154.00	6.54	25.67	1.20
23.03	150.00	23.80	13.00	1.20	112.00	4.71	8.62	1.34
23.05	155.00	23.75	12.00	1.25	118.00	4.97	9.83	1.31
24.12	165.00	24.10	13.00	1.90	126.00	5.23	9.69	1.31
36.29	170.00	25.20	19.00	1.80	124.00	4.92	6.53	1.37
36.30	190.00	24.10	10.00	1.90	154.00	6.39	15.40	1.23
38.00	160.00	22.80	4.00	1.20	132.00	5.79	33.00	1.21
38.06	150.00	22.30	2.00	1.70	124.00	5.56	62.00	1.21
38.39	160.00	22.60	2.00	1.40	134.00	5.93	67.00	1.19
38.41	155.00	23.15	8.00	1.85	122.00	5.27	15.25	1.27
53.60	155.00	23.45	10.00	1.55	120.00	5.12	12.00	1.29
53.86	195.00	25.25	18.00	1.75	150.00	5.94	8.33	1.30
54.02	185.00	23.80	8.00	1.20	152.00	6.39	19.00	1.22
54.27	190.00	24.00	9.00	1.00	156.00	6.50	17.33	1.22
57.64	165.00	22.85	3.00	1.15	138.00	6.04	46.00	1.20
58.72	170.00	23.65	9.00	1.35	136.00	5.75	15.11	1.25
82.10	150.00	22.40	2.00	1.60	124.00	5.54	62.00	1.21

Table 6: Sample Values – Composition is in moles x 1000								
Predicted Wear mg	MDI	T 1000	T 2000	TMP	BDO	BDO/T1000	BDO/T2000	MDI/BDO
82.33	180.00	23.20	3.00	1.80	152.00	6.55	50.67	1.18
84.18	180.00	23.85	9.00	1.15	146.00	6.12	16.22	1.23
84.31	160.00	22.85	4.00	1.15	132.00	5.78	33.00	1.21
85.02	200.00	24.75	14.00	1.25	160.00	6.46	11.43	1.25
123.38	160.00	23.20	7.00	1.80	128.00	5.52	18.29	1.25
126.15	150.00	22.50	2.00	1.50	124.00	5.51	62.00	1.21
127.52	200.00	25.45	19.00	1.55	154.00	6.05	8.11	1.30
127.63	195.00	23.60	4.00	1.40	166.00	7.03	41.50	1.17
129.27	195.00	23.50	2.00	1.50	168.00	7.15	84.00	1.16
184.87	175.00	24.95	17.00	1.05	132.00	5.29	7.76	1.33
184.87	170.00	24.40	14.00	1.60	130.00	5.33	9.29	1.31
184.93	170.00	24.10	12.00	1.90	132.00	5.48	11.00	1.29
185.89	190.00	25.40	19.00	1.60	144.00	5.67	7.58	1.32
186.19	195.00	23.65	4.00	1.35	166.00	7.02	41.50	1.17

Figure 31 shows predicted wear as a function of MDI composition and T2000. The effects of T1000 are similar while plots of wear and variations of BDO or ratios are less informative since the ratios are nearly constant as noted above. The particular graphing software does not provide easy to read 3D axes, so a contour plot of the values are shown in Figure 32.

EXAMPLES

The following examples are presented for illustrative purposes and are not intended to limit the scope of the claims which follow. Unless otherwise indicated, all parts are by weight, based on the weight of the final composition.

EXAMPLE 1

Preparation of Polymeric Biomaterials

Biomaterials of the present invention were provided in the form of polyurethane compositions having different compositions set forth in TABLE 7 below.

Table 7: Compositions of Various Suitable Biomaterials

Ingredient	**Compound A**	**Compound B**
	Weight %	Weight %
Isocyanate - diphenylmethane 4,4'-diisocyanate (also known as MDI, available from Bayer under the tradename Mondur M)	45.21	36.91
Polyol - polytetramethyleneetherglycol 1000 (as available from E.I. du Pont de Nemours and Co. under the tradename Terathane 1000)	23.80	-
Polyol - polytetramethyleneetherglycol 2000 (as available from E.I. du Pont de Nemours and Co. under the tradename Terathane 2000)	18.07	23.00
Polyol-Polytetrahydrofuran, molecular weight of 650, also known as PTHF 650 (also known as PTMO 650, as available from E.I. du Pont de Nemours and Co.)	-	23.04
Chain extender – 1,4-butanediol (as available from Sigma Aldrich Corp.)	12.69	8.14
Crosslinker- 2-ethyl-2-(hydroxymethyl)-1,3-propanediol (also known as trimethylolpropane, as available from Sigma Aldrich Corp.)	0.22	-
Catalyst- Bis-(dodecylthio)-dimethylstannane (available from Crompton Corp. as Fomrez catalyst UL-22)	0.0010	0.029
Antioxidant- Pentaerythritol Tetrakis (3-(3,5-di-tert-buyl-4-hydroxyphenyl)proprionate (available from Ciba Specialty Chemicals, Inc. as Irganox 1010)	-	0.49
Hydrophobic additive - hydroxyl-terminated Polybutadiene (Wq. Wt. = 550)(also known as Poly BD 20LM as available from	-	8.39

Ingredient	**Compound A**	**Compound B**
	Weight %	Weight %
Sartomer)		
Dye Green GLS (available from Clariant Corp.)	-	0.01
Total	100	100

As an example, a polymeric biomaterial having the composition of Compound A may be produced by making a prepolymer of all the ingredients listed above except 1,4-butanediol chain extender and Bis-(dodecylthio)-dimethylstannane catalyst. If desired, this prepolymer can be stored for later processing. The prepolymer can then be heated to approximately 25 °C, and mixed for approximately 30 seconds with the 1,4-butanediol chain extender and Bis-(dodecylthio)-dimethylstannane catalyst in a mixing machine using a volumetric ratio of approximately 6.25 prepolymer to 1,4-butanediol chain extender and Bis-(dodecylthio)-dimethylstannane catalyst. After mixing, the contents may be injection into a Teflon coated two part mold heated to approximately 160 °C to cure for approximately 30 minutes. After curing, the mold may be opened and the implant removed. The implant may be packaged, in packaging such as aluminum foil, and a vacuum may be applied to reduce contact between the implant and moisture in the air. The implant may then be placed in a dry oven for around 24 hours for annealing and post curing. The implant may then sterilized and packaged for delivery or use.

EXAMPLE 2

Comparative Properties

Various properties of Compounds A and B were determined and are compared in TABLE 8 provided below. As can be seen, Compound A, can be seen to provide improved and acceptable congruence and cushioning, as compared to Compound B, which provides properties that lead to improved congruence and cushioning and acceptable wear resistance. Hence Compounds A and B are particularly well suited to serve as the first and second biomaterials, respectively, of an interpositional arthroplasty device of this invention, and in turn, to provide a femoral glide path, and congruence tibial surface, respectively.

Table 8: Physical Properties of Various Suitable Biomaterials

	Compound A	**Compound B**
Abrasion	42 mm^3 dry > 5 million cycles on KMM	60 mm^3 dry
Compression Modulus	16,500 psi wet	4,780 psi wet
Compression Strength (not tested to failure)	> 8,320 psi wet	> 8,320 psi wet
Flexural fatigue resistance	> 5 million cycles	
Fracture toughness	Peak 128 lb wet Energy to break 45 lb-in wet	Peak 54 lb wet Energy to break 15 lb-in wet
Hardness	58 Shore D wet	84 Shore A dry & wet
Specific gravity	1.16 g/cm^3	1.11 g/cm^3
Tear Strength	920 PLI Die C dry 825 PLI Die C wet 256 PLI Die T dry 264 PLI Die T wet	429 PLI Die C wet 100 PLI Die T wet
Tensile Modulus 100% Elongation	3700 psi dry 3190 psi wet	
Tensile modulus 200% Elongation	5590 psi dry 4840 psi wet	2560 psi dry 1920 psi wet
Tensile strength	7800 psi dry 7130 psi wet	8300 psi dry 6900 psi wet
Ultimate elongation	295% dry 310% wet	650% dry 700% wet
Water absorption	1.2-2% by weight at 37C wet	1.6% by weight at 37C wet

EXAMPLE 3

Drug Loaded Polymer

The drug used in this Example was Gentamicin: Galipot. Polymer pieces were soaked for 4 hours in Tetrahydrofuran (THF) and overnight in antibiotic. The following extraction was performed:

Extraction: overnight	Inhibitory zone.

Controls for THF or THF and water-methanol treatments gave no inhibitory zone.

EXAMPLE 4

Drug Loaded Implant

In this example, a whole implant. (185 C) was swelled in THF for 4 hours and transferred to antibiotic solution for about 16 hours. The following extractions were made:

First extraction: 16 hours	Inhibitory zone
2nd Extraction: next 24 hours	Inhibitory zone
3rd Extraction: next 24 hours	Inhibitory zone
4th extraction: next 72 hours	Inhibitory zone
5th extraction: next 72 hours	No inhibitory zone

The quantification of the inhibitory zone of released antibiotic was measured by comparing it to that of standard antibiotic disks. A Sensi-Disc™ for Gentamicin (10 microgram/disc, Becton Dickinson) were used as standards. An antibiotic disc (10 microgram Gentamicin) was included on the plate on which the inhibitory zone of drug loaded implant pieces was being tested.

Numerous characteristics and advantages of the invention covered by this document have been set forth in the foregoing description. It will be understood, however, that this disclosure is, in many respects, only illustrative. Changes may be made in details, particularly in matters of shape, size and ordering of steps without exceeding the scope of the invention.